

# ARIZONA MEDICINE

Journal of ARIZONA MEDICAL ASSOCIATION

VOL. 11, NO. 2



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## *Original* ARTICLES

### SOME STUDIES ON GAS DISTENTION OF THE SMALL INTESTINE\*

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New York, New York

UNDER average normal conditions very little if any gas can be seen in the small intestine of adults on radiographs of the abdomen. This is presumably because swallowed air escaping from the stomach into the duodenum is efficiently absorbed before it progresses very far. In occasional instances, gas shadows can be seen beyond the duodenojejunal junction but the lumen thus outlined is the same width as that shown by barium in the normal intestine. Such gas shadows seem to be of no clinical significance.

Gas distention of the small intestine is, on the contrary, of great clinical importance. By gas distention is meant either (1) the presence of gas in several or many loops with no or very little increase in the width of the lumen over the average, or (2) widening of the gas-containing loop or loops definitely beyond the limits of normal, whether only one loop or several are involved.

The purpose of this paper is to present some examples of abnormal gas distention of the small intestine associated with either functional disorders or organic disease and to offer physiologic explanations for some of them.

#### NORMAL PHYSIOLOGY

Intestinal movements are commonly regarded as of two types: (1) the peristaltic or propulsive movements, and (2) the myogenic movements. In both, the longitudinal as well as the circular muscle coats play a part. The propulsive movements involving coordinated contraction and re-

laxation of the muscle are completely disorganized by cocaineization of the wall and are believed to be controlled by reflexes coordinated through the intramural nervous system. The myogenic movements continue unchanged after the intramural nerves are paralyzed and presumably are not controlled by them.

The small intestine is supplied by both divisions of the autonomic nervous system.

The PARASYMPATHETIC fibers arise from the right vagus nerve, pass through the celiac ganglion without synapsing, and accompany the mesenteric blood vessels to the intestine. In the intestinal wall the parasympathetic fibers synapse with nerve cells in both Auerbach's (myenteric) plexus, and in Meisner's (submucosal) plexus. The postganglionic fibers then continue to the end organs, either muscle or gland cells.

The SYMPATHETIC supply is derived from the splanchnics and makes a synapse in the celiac ganglion. The postganglionic fibers of the sympathetic pass with the mesenteric vessels to the intestine and are distributed throughout the wall to the end organs.

In the mesentery, therefore, are preganglionic parasympathetic and postganglionic sympathetic fibers.

The intramural nervous system is composed of both the myenteric and the submucosal plexuses which are elaborate networks of postganglionic sympathetic fibers, and pre- and postganglionic fibers and ganglion cells of the parasympathetic system.

Nerve degeneration experiments have given

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evidence that the intramural nervous system also contains fibers not of either sympathetic or parasympathetic origin. They appear to connect one short segment of intestine with another and presumably are the nerves through which the contraction and relaxation phases of the peristaltic movement are coordinated.

#### THE CHEMICAL MEDIATOR THEORY OF NERVE ACTION

This theory explains the mechanism of the effect of nerve stimulation on an effector cells as the result of a chemical substance produced at the nerve ending, rather than as the result of the nerve current itself. Loewi (1921) and Dale (1929) presented evidence that the stimulation of the parasympathetic fibers produced acetylcholine at the nerve endings. Cannon (1933) and others found that sympathetic stimulation produced a substance now called "adrenin" which is indistinguishable from the effects of epinephrine. It has been shown that the injection of acetylcholine or one of its derivatives into an animal produces the same effects as parasympathetic stimulation; these substances are called parasympathomimetic drugs. Acetylcholine is destroyed by a specific enzyme "acetylcholine esterase", which works very rapidly. This enzyme is inhibited or destroyed by certain substances, including prostigmine. The result of this inhibition of acetylcholine esterase is to intensify and prolong the effect of the acetylcholine which may be present, thus simulating the effect of parasympathetic stimulation or of the injection of acetylcholine. Obviously the "parasympathomimetic" effect of prostigmine could not be manifested unless acetylcholine were present. Acetylcholine is produced by an enzyme called choline acetylase in the presence of adenosine-triphosphate, thiamine, potassium ions (Nachmansohn and Machado), pantothenic acid (Jaques) and probably other substances. Nachmansohn and co-workers (1946) have shown that acetylcholine plays an important part in the transmission of nerve impulses along the axone and across the synapse as well as at the end-plate. The acetylcholine produced as the impulse passes must be destroyed very rapidly by acetylcholine esterase to restore the irritability of the nerve, otherwise the refractory stage is prolonged. Therefore failure to produce this substance, excessive destruction of it, or failure to destroy it at the right instant, would inter-

fere with the normal transmission of nerve impulses at various levels.

Stimulation of the parasympathetic nerves or the injection of acetylcholine or one of its derivatives increases the movement and the tonus of the small intestine. On the other hand stimulation of the sympathetic nerves or the injection of epinephrine, a sympathomimetic drug, inhibits the movements of the intestine and reduces tonus. The mechanism of this action of epinephrine is apparently not completely understood, but there is some evidence that it destroys or prevents the effect of acetylcholine, analogous to the effect of acetylcholine esterase. In fact, it has been shown that the continuous injection of epinephrine in dogs for 15 days produced a fatal gastrointestinal "inhibition" (Dragstedt 1934).

Not only the motor function but other functions of the intestine are under the influence of the nervous system, e.g. absorption and excretion through the intestinal wall.

#### GAS DISTENTION OF THE SMALL INTESTINE

The detection of gas distention of the intestine is dependent upon correct use of x-ray methods of examination. A film of the abdomen in the supine position usually suffices to show the presence of abnormal amounts of gas. To detect fluid levels in the distended loops, however, films made with horizontal rays are necessary, either with the patient erect or lying on either side.

Having shown gas distention of the intestine, the problem facing the radiologist is, if possible, to find an explanation for it.

Gas distention of the small intestine may be the result (1) of purely reflex causes arising either within the abdomen or outside it, (2) of disorders of neuromuscular physiology within the wall of the intestine, and (3) of organic disease of the intestine or mesentery.

#### GAS DISTENTION FROM REFLEX CAUSES

ILEUS may be defined as a dilatation of the small intestine, or a portion of it, associated with an accumulation of gas and fluid apparently resulting from excessive secretion and a failure of absorption, and with other disturbances in physiology. It is a "vicious circle" in that the greater the distention, the greater the disturbance in physiology and, therefore, more distention.

PARALYTIC ILEUS, as the term is ordinarily



used, is caused by some influence arising outside the intestine itself, which interferes with its ability to contract, to absorb gas etc. and thus starts the vicious circle of distention.

General peritonitis usually causes paralytic ileus. Considerable evidence has been presented that the distention caused by peritoneal inflammation is produced by excessive activity of the sympathetic system. Arai (1922) found that experimental peritonitis in cats produced a slowing of the gastric and intestinal movements. However, if the sympathetic fibers to the intestine had been previously cut no slowing occurred. Also if a parasympathomimetic drug (Choline) were injected in cats with intact nerve fibers, no slowing of the intestine occurred. Arai concluded that the effect of peritonitis on the intestine is the result of overstimulation of the sympathetics.

Di-isopropylfluorophosphate makes an irreversible combination with acetylcholine esterase, preventing the destruction of acetylcholine. Modell, Krop, Hitchcock and Riker (1946) found that the strong parasympathomimetic effect of this drug was prevented temporarily by epinephrine as well as by atropine. This, and other evidence, suggests that the inhibiting effect of epinephrine, and also of sympathetic stimulation, is produced by blocking the action of acetylcholine. Presumably the parasympathomimetic drug in Arai's experiments was sufficient to overcome the acetylcholine-blocking effect of the adrenin produced by the overstimulated sympathetic.

Banthine is a relatively new antiparasympathetic drug which produces (Longino and co-workers, 1950) an atropine-like postsynaptic block. It has been used to inhibit the secretion of acid in the stomach of patients with peptic ulcer. It also produces marked slowing of the transit time of the small intestine (Golden, 1950) and has been used at the Presbyterian Hospital (Lepore, Golden & Flood, 1951) in certain cases in which parasympathetic hyperactivity was present.

In two patients with ulcerative colitis, banthine caused gas distention of the small intestine. On patient discovered that he could control his abdominal distention by reducing the dose of banthine. It has long been known that rectal stimulation or irritation produces sympathetic effects. Ulcerative colitis involving the rectum provides a mechanism for sympathetic stimula-

tion. A hypothetical explanation for this distention with banthine would be the superimposition of sympathetic overactivity upon a parasympathetic block.

Gas distention of the intestine may appear in association with pneumonia and with lumbar myositis. In a healthy 18 year old boy extreme distention of the intestine and of the urinary bladder developed during an attack of very severe back pain, shown later to be the result of herniation of an intervertebral disc. This distention disappeared when the severe pain was relieved and recurred when he had a second attack of back pain. Both the distention of the bladder and of the intestine can be explained as the result of overactivity of the sympathetic.

#### GAS DISTENTION FROM DISORDER OF NEUROMUSCULAR PHYSIOLOGY

##### Hypoproteinemia.

For many years gas distention of the small intestine has been observed with hypoproteinemia, especially when large amounts of intravenous salt solution were given. This has occurred during the treatment of burns, following operations on the gastrointestinal tract, and as a complication of the treatment of mechanical ileus by deflation with the Miller-Abbott tube. After deflation is apparently complete, redistention along the Miller-Abbott tube may occur. According to the literature, edema begins to develop when the blood protein descends to 5.5 plus-minus 0.2 per cent. This distention is to be regarded as a mild paralytic ileus presumably the effect of edema of the wall of the intestine. The intestine does not respond to prostigmine which suggests a lack of acetylcholine in the intestinal wall.

##### Hypopotassemia.

Gas distention also occurs in some patients with a normal serum protein who have a low blood potassium. Moore (1949), and Randall and co-workers (1949) pointed out the association of intestinal distention with low blood potassium following surgical operations and in the presence of normal blood protein. These and other writers have shown that a loss of potassium occurs after operation which cannot be prevented during the first two postoperative days. Unless replacement of the K-ion is effected, the loss continues and symptoms develop in 4 to 9 days. These symptoms are drowsiness, languor, oliguria, edema and mild intestinal distention. Prostigmine has no effect on the distention, sug-

gesting a deficiency of acetylcholine in the wall of the intestine. The symptoms begin when the serum potassium descends to 3.5 meq/L (Normal 4 to 5 meq/L or 16 to 20 mgm/100 cc.) and become severe at 2.6 meq/L or less. The symptoms are quickly relieved by the administration of potassium and can be prevented if KCl is included in the intravenous infusions. The lack of acetylcholine can be reasonably attributed in part at least to the insufficiency of K-ions, which are necessary for its synthesis by choline acetylase.

#### Other Possible Causes of Insufficient Parasympathetic Effect

Occasionally gas distention is seen with both blood protein and potassium at normal levels. A 75 year old woman had a radical operation for carcinoma of the breast. Convalescence was normal until the 8th postoperative day, when gas distention of the intestine appeared. The blood protein and potassium were normal. Prostigmine produced no response in the intestine. After several days urecholine, an acetylcholine derivative, was administered parenterally and the distention promptly began to diminish and disappeared after 24 hours. The sequence of events suggests that for some unexplained reason production of acetylcholine was insufficient and after replacement by urecholine, the normal production of acetylcholine was restored. It seemed as if some sort of vicious circle had been interrupted.

Nothing was noted which would indicate what substance or substances necessary for the production of acetylcholine were lacking. It is known that adenosine triphosphate, a thiamine compound, the correct concentration of potassium ions and the enzyme choline acetylase are necessary for the production of acetylcholine. Jaques (1951) presented evidence that a diet deficient in pantothenic acid caused atony and distention of the gastrointestinal tract in rats and that the administration of pantothenic acid in 16 cases of paralytic ileus was followed by striking improvement. Nothing was said about the blood protein and potassium in Jaques' cases but the prompt clinical improvement suggests that neuromuscular physiology in the intestinal wall was improved after giving pantothenic acid, probably by increased production of acetylcholine.

It is quite possible that other substances as yet unidentified are necessary for the synthesis

of acetylcholine and may be lacking under certain conditions.

MECHANICAL ILEUS results from a mechanical interference with the transmission of intestinal contents. In many cases the obstruction was in existence for months or years and apparently the intestine was able to compensate for it. Then for some reason the compensation is broken, the intestine dilates and the vicious circle of ileus is established. For example, an annular carcinoma of the ileum suddenly produced an acute mechanical ileus in a 75-year old man who had been symptom free up to the onset of acute abdominal pain. After deflation with the Miller-Abbott tube, the lumen through the carcinoma was shown by barium studies to be not more than 3 mm. wide. At operation, extensive metastases were found in the liver, indicating that the carcinoma had been in existence for months or longer without causing symptoms, until the acute ileus developed suddenly. Adhesions may act in a similar way. Deflation of the intestine with the Miller-Abbott tube in ileus with peritoneal adhesions in some cases is followed by restoration of normal compensation without surgical release of the offending adhesion. It appears, therefore, that even in mechanical ileus there is a functional element.

#### GAS DISTENTION WITH ORGANIC DISEASE OF THE INTESTINE

##### Amyloidosis

Amyloidosis of the intestine may cause gas distention sufficient to simulate ileus (Randall, 1933). In a similar case sent to me by Dr. Powers of Palo Alto, California, histologic studies showed that the amyloid had been deposited in the myenteric ganglia, many of which had been destroyed (Golden, 1945, p.214). In a recent case at the Presbyterian Hospital gas distention of the small intestine over a period of several weeks with extremely slow passage of barium was due to amyloidosis. The blood protein and potassium were normal. The intestine did not respond to prostigmine, which suggested that insufficient acetylcholine was present. Then urecholine, a derivative of acetylcholine which has a marked stimulating effect on the intestine, was injected parenterally without noticeable effect on the small intestine. These facts suggested that for some reason the wall of the intestine was incapable of responding to acetylcholine and the possibility of amyloidosis was suggested.

### Scleroderma

When the digestive tract is involved by scleroderma, the esophagus is the most frequent location. Hale and Schatzki reported dilatation of the small intestine in four cases. In one of them, prostigmine and in another mecholyl (a derivative of acetylcholine) produced no effect. One patient developed the signs of mechanical ileus and at operation irregular dilatation of the upper loops of jejunum was found. In both amyloidosis and scleroderma the intestinal wall becomes incapable of responding to a parasympathomimetic drug.

### Sprue

In its advanced stages, the small intestine of victims of sprue shows evidence of submucosal edema, and of atrophy of the mucosa and of the tunica muscularis, (Golden, 1945, p. 91). This in some cases is associated with inability to absorb gas as well as other substances (Golden, 1945, p. 99). Kantor (1939) reported instances when the gas was sufficient in quantity to suggest ileus.

### DISEASE OF THE MESENTERY

Extreme dilatation and very slow movement of barium were found in the ileum of a 35 year old man. At operation extensive infiltration of the ileal mesentery by carcinoma metastases from a linitis plastica carcinoma of the stomach was found. The wall of the intestine was thickened and edematous but was not involved by the carcinoma. Re-examination six months after operation showed the lumen of the ileum to be normal in caliber. The patient died about sixteen months after the operation.

A hypothetical explanation of the dilatation of this intestine can be offered based upon Cannon's law of denervation, which is stated as follows: "When in a functional chain of neurones one of the elements is severed, the ensuing total or partial denervation of some of the subsequent elements in the chain causes a supersensitivity of all the distal elements, including those not denervated, and effectors if present, to the excitatory or inhibitory action of chemical agents and nerve impulses; the supersensitivity is greater for the links which immediately follow the cut neurones and decreases progressively for the more distal elements" (Cannon and Rosenblueth, 1949, p. 186). Assuming that the extensive infiltration of the mesentery by carcinoma could interrupt some of the neurones, par-

tial denervation could be produced. The mesentery contains preganglionic parasympathetic fibers and postganglionic sympathetic fibers. Therefore the sensitivity would be greater for the sympathetic chemical mediator which would result in dilatation of the intestine. Furthermore it has been shown in experimental animals that the hypersensitivity to epinephrine produced by denervation diminishes with the passage of time which would explain the return of the intestine to normal caliber six months after the operation.

Disease of the mesentery may also cause a localized dilatation of the intestine. In one instance it was due to a lymphangioma of the mesentery (Golden, 1945, p. 121), and in another to localized lymphadenitis and fibrosis of the mesentery in a case of regional enteritis (*ibid*, p. 141).

### DISCUSSION

Gas distention of the small intestine may occur in many different conditions. In some cases the reason for it may be easily found, if the basic physiology, particularly the neurophysiology of the intestine is borne in mind. The part played by acetylcholine, the factors concerned in its synthesis in the wall of the intestine, the antagonists of acetylcholine, the possibility of inhibition of the parasympathetic control by excessive sympathetic influence, — all of them are important concepts in the study of these cases.

Parasympathomimetic drugs are useful in the clinical investigation of selected cases. If a choline esterase inhibitor, such as prostigmine, fails to produce an effect on the intestine, a deficiency of acetylcholine may be hypothesized. If an acetylcholine derivative, such as urecholine or mecholyl, stimulates the intestine and reduces the dilatation, the above-mentioned hypothesis seems to be confirmed. On the contrary, if urecholine fails to produce an effect, the wall of the intestine is presumably unable to respond to the parasympathetic mediator substance, acetylcholine, which suggests organic disease of the wall. However, in some cases a reasonable explanation for gas distention cannot be found in the light of present knowledge.

The normal wall of the intestine is thin. When two gas-distended loops lie in contact, the space between the air columns should be 1-2 mm wide, which represents the width of the adjacent walls

of both. If this is 3-5 mm. in width, the wall is presumably widened by (1) edema, (2) disease of the wall such as amyloidosis, carcinomatosis of the peritoneum, tuberculous peritonitis, etc. Edema of the intestine is largely submucosal. It causes widening of the submucosa which extends into the mucosal folds. In the shadow of the gas-distended jejunum, these folds produce, in the absence of edema, sharply defined cross striations usually about 1 mm. in width. In the presence of submucosal edema, these cross striations become widened to 2-4 mm., and some become ill-defined. Ascites may separate two adjacent gas-distended loops.

#### SUMMARY

(1) Certain facts concerning the basic physiology of the small intestine are necessary to attempt to understand the significance of gas distention. Neuromuscular physiology, the chemical mediator theory of nerve action, and balance between the parasympathetic and the sympathetic divisions of the autonomic nervous system are of particular importance.

(2) Gas distention may result from purely neurogenic causes, from disorders of neuromuscular physiology within the wall produced by deficiency of one or more of the factors necessary for the production of acetylcholine, and from organic disease of the wall of the intestine or mesentery.

(3) Acetylcholine derivatives, such as urecholine and mecholyl, and acetylcholine esterase inhibitors such as prostigmine are useful in the physiologic study of selected cases.

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## CLINICAL EXPERIENCE WITH THE ARTIFICIAL KIDNEY AND RELATED PROCEDURES

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**D**URING the past ten years a number of procedures have been developed which have one characteristic in common: They remove large volumes of blood from a patient; this blood is modified outside the patients' body and is then returned. Several of these procedures have now been used in over one thousand instances and it is the general opinion among those who are well acquainted with these methods that blood dialysis ("the artificial kidney") and certain other related methods have a useful and well defined place in the medical armamentarium, and that these procedures have outgrown their infancy

and should not now be regarded as experimental treatments. This paper aims to describe some of the clinical experience with dialysis and similar methods and to outline the indications and contraindications for their use.

When the natural homeostatic mechanisms have become inadequate in a patient it may be desirable by way of treatment to accomplish one or several of the following purposes: to add to or remove from the body substances which may be deficient or which may be present in excess. Such substances could be easily diffusible, small molecules (electrolytes, glucose, water, the unknown toxins which cause certain symptoms of uremia), they may be the size of



protein molecules or bound to protein molecules, or they may even be cellular constituents of the blood or bound to blood cells. Accordingly, when it is necessary to remove blood cells such as in fetal erythroblastosis, the patients' blood can be taken off in toto and may be replaced with normal bank blood. Such a procedure is called *replacement transfusion*. In certain instances the blood of a sick patient is passed through the body of a healthy donor, so that the patients' blood and that of the donor are completely admixed; this procedure is called *cross transfusion* and presupposes that the intact organs of the donor can furnish deficient materials to the patient and dispose of accumulated waste products with impunity. In certain conditions in which the existence of toxic proteins may be a factor in the causation of disease it may be desirable to modify the blood in such a way that the patients' own blood cells are returned to him while the blood plasma is removed intermittently or continuously. This procedure is called *plasma replacement* or *plasmapheresis*. Finally, it is often beneficial to return the patients' plasma proteins and blood cells, while removing or adding small, diffusible molecules. This can be accomplished by the various methods of blood *dialysis*, which have been called "*the artificial kidney*" when a dialyzing solution is used to modify the patients' blood and "*artificial placenta*" when whole blood is used in place of the dialyzing solution, as has been done in some instances ("placenta" not because it imitates or replaces this organ, but because it is like a placenta in structure: blood — membrane — blood). Only those procedures which have become well established in American medical practice and are therefore not considered experimental will be mentioned here, although it should be pointed out that some of the other treatments have also had extensive clinical application here and abroad.

Of the above methods the *artificial kidney* has had the widest use and the most extensive bibliography. This procedure uses commercially available cellophane membrane to "wash" the blood. The sieve-like pores in a cellophane membrane readily permit the passage of molecules or ions up to a weight of 4000. Larger particles, cells, bacteria and viruses do not pass through the membrane. This membrane comes in the form of sheets or tubes; it can be used as a series of sheets which are held in place by

plastic or rubber pads, or as coiled tubing which is wound on horizontal or vertical drums which may or may not rotate. The clinical response to dialysis is influenced by the kind of cellophane, the method of its mounting and the nature of the dialyzing solution. This fact is not often realized and may account for some of the clinical disparities.

During an actual dialysis the patient is heparinized. Blood is removed from an artery or vein at a rate of about 200 cc. per minute. The blood is routed through the sterile dialyzer and returned to the patient. This procedure may be continued until the desired result is achieved which will usually be the case after 6-8 hours of dialysis. The dialyzing apparatus should be capable of removing about 80-90% of the identifiable waste material (urea, creatinine) in one passage of blood through the machine; this is accomplished with 40,000 sq. cm. of cellophane tubing in the Kolff-Harvard type of machine and with about 21,000 sq. cm. of cellophane in the Skeggs-Leonards model. Both devices have a "urea clearance" of up to 180 cc. per minute and a "creatinine clearance" of up to 120 cc. Untoward side effects have not been observed from the use of the sheet cellophane dialyzer described by Skeggs and Leonards; but the use of the Kolff-Harvard machine causes elevations of blood pressure in about 25-30% of the patients. It is possible that this complication indicates constriction of the renal arterioles caused by the passage of blood through cellophane tubing; such vasoconstriction may even interfere with the natural repair processes in the kidney and could well be responsible for the fact that many patients exhibit excellent "chemical" results from the dialysis treatment (lowered blood NPN, adjusted electrolyte balance, diminished edema) but do not show a corresponding prolongation of their life span. In the future it may be possible to avoid such constriction of the renal arterioles during dialysis either by using the sheet cellophane dialyzer of Skeggs and Leonards or by using the renal vasodilator hydrazinophthalazine ("Apresoline" (R)). Other serious complications of artificial kidney treatment have not been observed in a significant number of cases, but it is obvious that the method cannot be used in the presence of gross hemorrhage because of the need for heparin. During the course of dialysis the patients do not usually require additional

medication, and there is no discomfort due to the procedure.

The method is very effective in adjusting derangements of the electrolyte levels such as hyperkalemia (excessive potassium), in reversing or mitigating some of the clinical features of uremia — coma, nausea, twitching and the like — in removing diffusible poisons such as barbiturates or bromides, and in treating pulmonary and peripheral edema of varied etiology. \*

From the clinical point of view it is up to the attending physician to decide whether or not dialysis or some similar method should be used in an individual case. His judgment will be influenced by the availability of the apparatus and experienced operators, the adequacy of the preceding conservative treatment, and the prognosis of the case. It should be emphasized that many patients who a few years ago were considered to be beyond hope can now be reclaimed by careful conservative management. This is especially true for patients with anuria or oliguria, the syndrome which used to be called "lower nephron nephrosis" and which is now known as acute renal failure. There is no hard and fast rule which one should follow in the selection of anuric patients for dialysis treatment. In general, the clinical condition of the patient is the most valid criterion; W. J. Kolff, one of the originators of dialysis, will dialyze an anuric patient "whenever I'm scared not to do so." Increasing mental confusion, coma, increasing left heart failure and pulmonary edema, and hyperkalemia are primary indications for the immediate use of dialysis in the uremic patient, but of course, do not substitute for careful conservative management before and after the dialysis, including the use of potassium-absorbing resins by mouth, the rigid control of water balance, etc.

At the University of Minnesota it was possible to keep an anuric child alive for ninety-one days with the combined use of dialysis and of conservative measures; the child was then permitted to die because the underlying lesion (severe glomerulonephritis) was deemed to be beyond repair. The case illustrates the therapeutic possibilities of dialysis in anuric patients, inasmuch as the longest recorded survival of anuric patients under conservative treatment alone is only about 25 days.

In one of our cases, M. W., a 15 year old boy, became anuric following an episode of massive

bilateral hemorrhage from both ureters apparently due to some form of purpura. The anuria continued for six days, the patient became mentally confused and developed severe pulmonary edema in spite of careful management and the avoidance of overhydration. During a dialysis procedure which lasted 8 hours, 2500 cc. liquid was removed from his blood and the blood creatinine lowered from 14 to about 9 mgm%. Following the procedure the patient was mentally clear, pulmonary edema had disappeared, peripheral edema decreased, and the next day he started to diurese. There was an uneventful recovery and the procedure was considered life saving.

The following case illustrates the use of dialysis in a case of uremia due to chronic glomerulonephritis. M. F. a 48 year old married nurse, had been known to suffer from glomerulonephritis of the one kidney which remained after unilateral nephrectomy 30 years ago. She was hospitalized for three months before the dialysis procedure, the reason for hospital care was the fact that she was nauseated to a degree which made it impossible for her to retain even small quantities of liquid or solid food. She received all liquids intravenously or by subcutaneous clysis during a period of three months, was suffering intensely from headaches as well as nausea and maintained a blood creatinine level of about 12 mgm%. The continued hospitalization constituted a severe drain on the family budget.

Following a dialysis procedure her blood creatinine decreased to 5 mgm%, but returned to the earlier high level within the week; however her nausea and headache disappeared immediately after the dialysis and she was able to eat and retain solid as well as liquid nourishment. Ten days after the dialysis she was discharged from the hospital and was able to do her housework at home, where she lived for seven months before she died from a severe intercurrent bilateral pneumonia.

There are now many cases of patients with chronic irreversible uremia who have been made and kept comfortable by dialysis, even though it is not claimed that their life span has been increased by this procedure. The majority of these patients have been treated with the Kolff-Harvard type of dialyzer and one wonders whether or not the use of apresoline with the dialyzer or the use of the Skeggs-Leonards

dialyzer would not have yielded even better clinical results. It is quite possible that the more modern techniques of dialysis will indicate a wider and more varied usefulness of this principle.

Recent experiments have furnished evidence that dialysis is able to remove barbiturates from the blood about twenty times as rapidly as the intact hepatorenal system of a patient. This would seem to make dialysis the treatment of choice in cases of severe barbiturate poisoning. I have no clinical experience with this type of patient, but have recently seen a dog, weighing 33 pounds, which had received 1800 mgm (30 grains) sodium phenobarbital intraperitoneally. This dose corresponds to 200  $\frac{1}{2}$  grain phenobarbital tablets in a 130 pound person. The dog woke up after only 3  $\frac{1}{2}$  hours of treatment with the artificial kidney, indicating that similar instances of barbiturate poisoning can be treated very effectively in human patients; as has been reported from a group in Washington, D. C.

A few remarks about published statistics may be in order here. When one reads publications which describe a series of patients who have been treated with the artificial kidney one is impressed by the fact that these patients are not expected to live when treated with conservative methods alone and that the patients are suffering from a wide variety of pathological states. Moreover, the dialysis procedure varies with each operator and is not well standardized. Different operators employ differing solutions, differing machines, differing criteria, and differing auxiliary treatment. It is not surprising therefore that the results of the application of the artificial kidney have varied greatly and that in some hands it has yielded gratifying results while the clinical effect in other centers has been almost zero and has tended to discredit the procedure. Many encouraging successes have been reported wherever the artificial kidney procedure has been used in time, and not as a last ditch heroic measure. The procedure has been very welcome in the Army Hospital in Pusan, Korea, at the Peter Bent Brigham Hospital in Boston, at the Cleveland Clinic and the New York Hospital. At the University of Minnesota and at the Southwestern Medical School in Dallas the procedure has been tried but encouraging clinical results have not been observed. It is believed that this discrepancy must be due to variations in the technique used

at these centers, because even slight variations may make the difference between success and failure. For instance, when first used in Dallas, dialysis was tried on patients without being first tested on animals. Later studies showed that, as practised in Dallas, dialysis actually shortened the life span of treated uremic dogs. Dialysis was therefore abandoned. It is interesting to note that the method has been recently revived in Dallas, and with more adequate equipment. When one is engaged in the treatment of patients who have been given up by everyone else one cannot expect to be successful every time, but those patients who are salvaged or who are made comfortable for prolonged periods of time make the procedure worthwhile and compensate the operator for the times when the procedure proves to be a heroic but fruitless effort.

*Replacement transfusion* has been used in several hundred patients who had diseases other than erythroblastosis fetalis. It has the advantage that complex equipment is not necessary and that it can be performed wherever large amounts of blood are available from a blood bank. Blood is removed from the patient's radial artery or from his saphenous vein. Simultaneously with the removal, corresponding amounts of bank blood are injected into a peripheral vein. The infused blood should be cross matched very accurately, since intravascular hemolysis may aggravate the already precarious condition of the patients. During the procedure the patient should receive about 10 cc. of calcium gluconate intravenously for every four units of blood given. The procedure often causes allergic phenomena such as urticarial wheals, which can be controlled by intravenous antihistaminics. Some patients will require intravenous sedation during this procedure, because they may become frightened by the appearance of hives and itching, by the sight and handling of large amounts of blood, etc.; One should aim to remove a quantity of blood corresponding to about twice the total blood volume of the patient. Replacement transfusion will then dilute the patients' own blood so as to leave only about 15% of the original plasma and red cells in the patients body.

Replacement transfusion is the method of choice when it is necessary to remove non-diffusible substances from the blood stream, such as the toxin produced by *Clostridium Welchii*, the



complexes of carbon monoxide and hemoglobin, large amounts of free hemoglobin etc. The literature contains reports of about twenty patients who were successfully treated with replacement transfusion for anuria due to clostridium infections. Since one can only remove small amounts of diffusible substances with replacement transfusions the use of this method would seem to be a waste of blood when other effective methods for heroic treatment are available. It must be borne in mind, however, that much is yet unknown about renal physiology, the nature of the toxic substances in renal disease and the efficacy of various therapeutic measures. When no other treatment is available it would seem justifiable to use this method. Some physicians, like Snapper of Chicago, prefer this method in the treatment of anuria to the use of dialysis; it must be noted however that Snapper had experience only with the obsolete models of the artificial kidney.

The following case is of interest because it illustrates the surprising results which one sometimes encounters in this field. G. F., was a 40 year old Baptist minister with six children. During a physical examination 20 years ago he was informed of the presence of albumin in the urine. Whenever he had a physical checkup in the intervening period he was again told of the abnormal urine, but he continued to work and to lead a normal life until 1951 when he developed symptoms of uremia. He became weak and nauseated, suffered from severe headaches, anemia developed and he lost much weight. He was hospitalized for several weeks and had all known treatments, including repeated transfusions of washed red cells. In June 1952 his blood creatinine was 15 mgm%, the creatinine clearance was 5.5% of normal, he exhibited involuntary twitchings and was advised by several other physicians that he was in the terminal phase of

uremia. Although I felt that I probably would not be able to offer any constructive help I consented to treat him because on the flat abdominal x-ray plate his kidneys did not appear very contracted and his blood pressure was only moderately elevated — 160/110. It is hard to turn down a person who comes to you for help unless all the facts are clearly against the patient; one cannot always predict the outcome in the individual case. On June 4, 1952 9,000 cc. of his blood was withdrawn and 9,800 cc. was administered. Immediately after the replacement transfusion he felt much stronger, the uremic signs and symptoms disappeared and the creatinine clearance rose to about 10% of normal. Four weeks after the procedure he resumed his work as a minister and has since been working steadily and without symptoms on the same protein — poor regime which he had followed for years before. When last seen about two weeks ago he was still asymptomatic and working, although his serum creatinine had risen to 12 mgm% from the 8mgm% immediately after the transfusion. One would find it hard to explain the limited therapeutic success in this case unless one postulates the existence of toxic proteins in this man's blood, which may have been removed by the replacement transfusion.

In our hands the procedures of dialysis and related measures have yielded favorable results in about half of the cases. We have never regretted their use but, on the contrary, have had occasion to regret their omission in several patients who seemed to respond well to conservative measures but died when diuresis had already set in. I feel confident that these procedures will eventually stand the test of time and will be accepted for what they are — valuable additions to the armamentarium, which enable us to prolong the life and productivity of many otherwise hopelessly ill patients.

## CANCER OF THE OVARY

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**I** WILL discuss cancer of the ovary from the standpoint of a therapeutic radiologist.

In my experience, radium therapy seldom is indicated for the treatment of ovarian cancers, with the possible exception of implanting

needles or radon seeds in recurrent nodules which sometimes develop in the abdominal scar following operation, or for extensions or metastases into the vaginal wall.

However, roentgen therapy plays an important role in the treatment of malignant neoplasms



of the ovary, principally as an adjunct to surgical procedures. Roentgen therapy should be employed under the following conditions (1) if complete removal of all malignant tissues is impossible or found to be improbable; (2) as a pre-operative procedure for certain types of ovarian cancers to reduce the extent of involvement so that in certain selected cases surgical procedures may be performed for palliation; (3) for advanced cancer of the ovary involving the pelvic or abdominal structures extensively. I doubt that pre-operative irradiation will render what was primarily and inoperable condition surgically curable.

The diagnosis of malignant tumors of the ovary is not easy. They develop insidiously, usually in women in the middle age group approaching the menopause. In many instances the first manifestation will be slow, progressive enlargement of the abdomen, often attributed to so-called "middle age spread", or even pregnancy. There may be no obvious tumor mass if the abdominal enlargement is due to ascites. This sign of malignant growth develops so slowly that it may be unrecognized for some time, either by the patient or by the physician. Bimanual pelvic examination should be made under such circumstances; also, peritonescopy is a most valuable diagnostic procedure. Vaginal bleeding does not occur frequently, but may develop if there is extensive, invasive growth. Some malignant tumors of the ovary may be quite limited, but others rapidly invade the adnexa, neighboring viscera and spread by lymphatic channels and blood stream to result in remote metastases. Therefore, not infrequently the signs and symptoms of ovarian cancers will be caused by involvement of one or both ovaries, the uterus, vagina, peritoneum and rectum. In addition to abdominal enlargement, a frequent symptom is pelvic or lumbar pain due to the pressure of a tumor or invasion of pelvic structures. There may be secondary anemia, weakness and weight loss in advanced cases. The most frequent sites for metastases to appear outside of the abdomen are in the lungs and brain.

About 25% of primary tumors of the ovary are malignant. Carcinomas of several clinical and histologic types are most common; sarcomas being uncommon. The carcinomas may be cystic or solid. The different types and their treatment will be discussed individually. How-

ever, in general, it is my opinion that radical surgery is indicated as the primary treatment in most cases. Whenever possible, the primary ovarian tumor, both ovaries and the uterus should be removed. According to my observation, the so-called "all American operation" or "pelvic exenteration" is of doubtful benefit because of the necessarily high mortality and morbidity.

**Papillary adenocarcinomas of the cystic type** are the most common of the malignant ovarian neoplasms. As in other glandular organs, malignant degeneration may develop in a cyst which primarily may have been benign. These neoplasms sometimes are bilateral, usually grow quite rapidly after breaking through their cyst wall, then invade other pelvic structures and become implanted on the peritoneum and cause ascites.

Tumors of this type are relatively radio-sensitive. Roentgen therapy should be given immediately after the operation, when the cyst wall has been ruptured spontaneously or at operation or if invasion of the surrounding structures is found. The treatment may not cure, but usually delays the formation of ascitic fluid, alleviates distressing symptoms and prolongs economic usefulness and life.

When ascites has already developed from an extensive invasion of the peritoneum, roentgen therapy should be given after paracentesis which is necessary because the fluid will absorb so much of the radiation that otherwise the neoplastic tissues cannot be adequately irradiated. I doubt that under such circumstances surgical procedures will be beneficial so far as the removal of much malignant tissue is concerned.

I have tried intra-abdominal injection of radio-active gold (Au 139), after paracentesis, in some patients with far advanced papillary cystadenocarcinoma of the ovaries with ascites. The only effect observed was possible delay of the formation of ascitic fluid in a few instances, comparable to similar benefit from roentgen therapy. This occurred only in patients when the radio-active material could be diffused homogeneously throughout the peritoneal cavity. When there was loculation, it was impossible to give adequate and homogeneous irradiation with the isotope. The results were disappointing.

**Papillary adenocarcinomas of the solid type** are extremely malignant and progress rapidly.

The primary tumors vary in size, but most of them, when not checked, will occupy not only the pelvic cavity, but also extend into the abdomen. If these tumors are small, they may be removed surgically, but roentgen therapy should always be given post-operatively because of their high degree of malignancy. They are quite radio-sensitive. Even when recurrences develop subsequent to operation and irradiation, it may be advisable to operate again if there are no remote metastases, to remove as much malignant tissue as possible, and then give more roentgen therapy depending upon the dosage given previously and to the present condition of the tissues irradiated.

**Adenocarcinomas** of the ovary of the pure solid type are uncommon, but are the most common of the solid variety of ovarian cancers. They may be unilocular or multilocular. Most can be removed completely by surgery, but it is wise to give roentgen therapy post-operatively as a "prophylactic" procedure, because neoplastic cells may have invade neighboring tissues or escaped the most meticulous surgical technique.

**Glandulosa cell carcinomas** are low-grade, slowly growing neoplasms with variable hormonal influences. Usually the normal menstrual cycle is altered, but otherwise there seems to be no characteristic symptom except pelvic mass. Many of these tumors can be removed surgically, and cured if limited in size. However, if invasion into surrounding tissues is encountered, radical operation is necessary, to be followed by roentgen therapy, though these neoplasms are not particularly radio-sensitive.

**Arrhenoblastomas** of the ovary are also solid tumors showing active hormonal influences, causing masculinization of varying degree. Frequently atrophy of the uterus occurs. They are relatively rare, often unilateral, rarely metastasizing and are one of the lowest grades so far as malignancy is concerned. The treatment is surgical. Post-operative roentgen therapy seldom is beneficial, but it may be worthwhile in exceptional cases when a high degree of malignancy may have been found histologically.

**Dysgerminomas** also are rare. They are composed of undifferentiated sexual elements which I have always thought of as similar to seminomas of the testicle. They are similarly radio-sensitive and responsive. They appear in the younger age groups, usually between twenty and thirty.

They also affect endocrine balance, therefore, it is not unusual for the Aschheim-Zondek test to be positive.

These tumors often are found to be bilateral; extremely invasive of surrounding pelvic structures. They metastasize early and widely, especially to the lungs. Post-operative roentgen therapy is indicated, not only locally, but to the abdominal or aortic lymph node drainage as well, or to remote metastases when demonstrable.

**Teratomas** of the ovary may be cystic or solid, and are similar to teratomas of the testicle and may metastasize by way of the blood stream. They usually occur in young females, occasionally in children. The symptoms produced are due to pressure pain of the mass in the pelvis. Sometimes slight vaginal bleeding may occur. In contrast to the cystic type, the solid type of teratoma may be malignant, being composed of several types of adult and embryonal components. The adult formations are similar to dermoids, developing either unilaterally or bilaterally, and are often pedunculated, and therefore not difficult to remove. Most of these tumors are definitely radio-resistant, except those composed largely of embryonal forms. Since most have both adult and embryonic tissues, the latter be responsible to irradiation are quite variable, depending upon the histologic composition of the primary or metastatic growth. Of course, operation is necessary. Immediate post-operative roentgen therapy is of doubtful benefit, though it may be necessary for the rapidly growing embryonal forms or for metastases.

**Sarcomas** of the ovary are quite uncommon and of several different histologic types, developing from the interstitial tissues. They may occur at any age and usually present symptoms and signs of pressure within the pelvic cavity. They can often be cured surgically because of their limited growth. Roentgen therapy may be necessary if there is extension, if post-operative recurrence develops or for remote metastases for palliation.

**Krukenburg** tumors are associated with primary malignant tumors of the gastro-intestinal tract. These neoplasms are not primary in the ovary, but metastatic. Treatment is surgical, including removal of the pelvic mass and primary tumor, if possible. Roentgen therapy is of little or no benefit for these metastatic neo-

plams.

Patients to be given roentgen therapy for cancer of the ovary must be individualized. There can be no standard technique or dosage. The radiologist is responsible for the procedure. He must give consideration to the type of growth; its extent; and the physical condition and size of the patient.

Many types of roentgen therapy apparatus are available, the most common being in the range of 200 kilovolts, which is satisfactory for most cases. The supervoltage types offer only greater quantity of rays of higher penetrability. There is nothing unique or mysterious about their carcinoidal effects. Nevertheless, such apparatus is an advancement in the treatment of deep seated malignant conditions, but it has limita-

tions. A primary growth may be destroyed by irradiation, but when the disease has become disseminated, not even the most powerful apparatus will effect a cure.

In conclusion, in my opinion the treatment of ovarian cancer is primarily surgical and roentgen therapy is a valuable adjunct because:

(1) the diagnosis of ovarian malignant neoplasms often is difficult and the type and extent of the disease often cannot be determined until surgical exploration and histologic examinations have been made;

(2) because it is essential for the radiologist to know the type and extent of the disease before deciding upon whether or not irradiation may be beneficial, and how it should be given, if indicated.

### DEMEROL<sup>(R)</sup> AS AN ANTI-SCORPION THERAPEUTIC AGENT

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**I**N recent years, several children who died from apparent scorpion envenomization had received Demerol<sup>(R)</sup> as a therapeutic agent. In addition to this, it was observed that some of these children had not reacted in a manner typical of a child who has received a lethal dose of this venom. These combined observations suggested the need for an investigation into the combined effect of Demerol<sup>(R)</sup> and *Centruroides sculpturatus* Ewing scorpion venom in the mammal.

#### MATERIALS AND PROCEDURE

Mature, albino rats were used as the experimental animals, because the reaction of this animal to *C. sculpturatus* venom parallels that of the child very closely. The therapeutic agent tested was Demerol<sup>(R)</sup> solution containing 50 mg. per milliliter.

In order to get a sufficiently wide range of action, three groups of rats were given respectively, .18 mg., .15 mg., .10 mg., per 100 gram body weight of *C. sculpturatus* venom. The rats of each group then were given respectively, 20 mg., 15 mg., 5 mg., 2 mg., 1 mg. of Demerol<sup>(R)</sup>. In order to determine a lethal dose of Demerol<sup>(R)</sup> on these animals control animals were given the following series of dosages: 40 mg., 30 mg., 25 mg., 20 mg., 15 mg., 10 mg., per 100 gram body weight.

In each test animal the venom was first in-

jected and immediately followed with Demerol<sup>(R)</sup>. Both were administered subcutaneously in the groin.

#### RESULTS

All the venom used throughout the experiment came from lot number 62-73, whose LD<sub>50</sub> was .15 mg. per 100 gram body weight of the albino rat. Out of the ten rats used, fifty per cent given this venom recovered, while the lethal-time for those that succumbed averaged approximately 80 minutes. An approximate MLD for Demerol<sup>(R)</sup> was established at 25 mg. per 100 gram rat body weight. At this dosage, the lethal-time ranged from 37 to 91 minutes. All rats given only 20 mg. per 100 gram body weight, or less, recovered.

From the accompanying table, we may observe the following: (Table on page 52.).

1. In the 0.18 mg. group of rats, the lethal-time is shorter for those rats receiving from 5 to 20 mg. of Demerol<sup>(R)</sup> than for those receiving no Demerol<sup>(R)</sup>.
2. In the LD<sub>50</sub> group (0.15 mg.), all rats receiving Demerol<sup>(R)</sup> died, whereas, if the therapeutic agent had no untoward effect, only 50 per cent of the animals should have succumbed. In addition to this, the lethal-time averaged less than 32 minutes, in contrast to 80 minutes for the rats receiving only venom.

\*Assisted by M. J. Hagler.

3. In the 0.10 mg. group of rats, only one recovered, whereas all should have recovered. Also, the lethal-time average is 50 minutes, less than the lethal-time of the LD<sub>50</sub> rats.

**EFFECT OF VARYING DOSAGES OF DEMEROL<sup>(R)</sup> AND CENTRUROIDES SCULPTURATUS VENOM ON THE ALBINO RAT**

Rat Weight In Grams	Venom mg/100g Body Wgt.	Demerol(R) mg/100g Body Wgt.	Lethal Time*
179	0.18	none	45
314	0.18	none	37
152	0.18	20.0	20
173	0.18	15.0	30
129	0.18	10.0	26
216	0.18	5.0	35
189	0.18	2.0	59
168	0.18	1.0	60
166	0.18	0.5	103
190	0.15	20.0	10
314	0.15	20.0	31
129	0.15	15.0	29
269	0.15	15.0	7
219	0.15	10.0	53
171	0.15	5.0	53
183	0.15	2.0	44
248	0.15	1.0	27
241	0.10	none	Recovered
191	0.10	20.0	18
265	0.10	15.0	88
246	0.10	10.0	63
235	0.10	5.0	37
241	0.10	2.0	46
171	0.10	1.0	Recovered

\*Elapsed time in minutes from injection of venom and/or Demerol(R) until death.

While determining the lethal dose of Demerol<sup>(R)</sup>, we were greatly impressed by the similarity of symptoms produced by it to those produced by *C. sculpturatus* poisoning.

**CONCLUSIONS**

Demerol<sup>(R)</sup> appears to act synergistically with *Centruroides sculpturatus* venom in producing a lethal effect on albino rats. Consequently, Demerol<sup>(R)</sup> should be considered as contraindicated as a therapeutic agent for individuals under the influence of *Centruroides sculpturatus* scorpion venom.

**SUMMARY**

Albino rats given Demerol<sup>(R)</sup> after being envenomized by *Centruroides sculpturatus* scorpion toxin died more rapidly than when given either substance alone.

Those given a definite lethal dose (0.18 mg per 100 gram body weight) died more quickly with Demerol<sup>(R)</sup> dosages from 5 to 20 mg. per 100 gram body weight than those receiving venom alone. Rats given an LD<sub>50</sub> followed by Demerol<sup>(R)</sup> of 1 to 20 mg. dosage all died, whereas theoretically without Demerol<sup>(R)</sup> only 50 per cent should have died. Those rats given a sublethal dose of venom followed by Demerol<sup>(R)</sup> all succumbed except one, which received only 1 mg. of the supposed therapeutic agent. Parts of the syndrome of a lethal dose of Demerol<sup>(R)</sup> closely parallel that produced by *Centruroides sculpturatus* venom. From the results obtained, it is concluded that it would be unwise to administer Demerol<sup>(R)</sup> to a mammal envenomized with *Centruroides sculpturatus* toxin because of an apparent synergistic action between the two agents.

## PHOENIX *Clinical* CLUB

The Case History in this discussion is selected from the Case Records of the Massachusetts General Hospital, and reprinted from the New England Journal of Medicine. The discussant under Differential Diagnosis is a member of the staff of the Massachusetts General Hospital. The other discussants are members of the Phoenix Clinical Club.

### CASE RECORD NO. 1

A twenty-three month old Portuguese-American girl was admitted to the hospital because of dark

colored urine.

One week before entry she began to void dark urine and to pass light-colored stools. For two days previous to entry, she was feverish, and it was noted that the abdomen was enlarged. She had no vomiting, diarrhea or other systemic or constitutional symptoms.

The family history was not contributory. The patient was a full-term, normally delivered infant who had received an adequate diet and had



undergone normal growth and development.

Physical examination:—A well developed and well-nourished child whose breathing was rapid and shallow, but regular. There was moderate icterus of the skin and sclerae. Shotty lymph nodes were palpable bilaterally in the cervical and inguinal regions. The heart and lungs were normal. The abdomen was protuberant and tense. The liver edge was palpable at the level of the umbilicus. There was no spasm or tenderness. The spleen and kidneys were not palpable and no fluid wave was obtained. Examination of the nervous system was negative.

Temperature 99.6, pulse 140, respirations 28.

Several samples of urine were deep brown, with moderate amounts of bile. There were slight traces of albumin on several occasions with repeatedly negative sediments. The urine was free of urobilinogen. Blood:—RBC, 3,560,000 to 5,100,000, with corresponding Hgb. determinations between 69 and 83%; white counts between 13,000 and 19,000 with normal differentials. Blood Hinton negative. Repeated blood cultures negative. Venous clotting time 7 minutes, with a normal clot retraction. Fasting blood sugar was 182 mg. per 100 cc.; blood cholesterol 268 mg. The van den Bergh reaction was biphasic; the NPN of blood serum was 28.7 mgm. The stools were constantly clay colored. Repeated brucellergin tests and tuberculin tests in dilutions up to 1:10 were negative. Investigation of sputum for fungi was negative.

Roentgenograms of the skull and extremities were negative, and those of the lungs showed a moderate amount of diffuse, fine, mottled peribronchial infiltration. On repeated examinations of the chest, the infiltration became more diffuse over a two week period and then remained unchanged until three months later, when the lung fields became more vesicular and emphysematous.

The patient remained in the hospital for four months. During this time she ran an intermittent lowgrade temperature, with occasional bouts of fever up to 103 F. Her condition remained essentially unchanged except for a slight but steadily progressive loss of weight. Jaundice persisted. Two and a half weeks after entry, the spleen became palpable. Three and a half months after entry, a lymph node biopsy was interpreted as showing chronic nonspecific lymphadenitis. Four months after admission, an exploratory laparotomy was performed. Al-

though the patient apparently withstood the procedure quite well, death occurred on the first postoperative day.

#### CASE NO. 1-A

In June, 1946, at 30 years of age, a male clerk first came under hospital care at another institution, complaining of severe thirst, urinary frequency and polyuria, and loss of appetite, strength, & weight.

Seven years earlier, in 1939, he had received surgical care for an infection of a foot, the exact nature of which is not known. At that time, and for several years thereafter, he was employed as a metal grinder. In 1942 he was first troubled by a chronic discharge from the right ear, and by a disorder of the scalp diagnosed as seborrheic dermatitis. He served with the Navy between 1943 and 1945, spending six months of that period in the South Pacific. His only illness during that time was a fever of unknown etiology lasting 2 days.

His present illness began in April, 1946, with insidious onset of increasing thirst, polyuria and nocturia. Within three weeks he experienced loss of appetite and strength. At the time of his first hospital admission in June, 1946, he had lost 7 lbs. in weight and was consuming six quarts of fluids daily. On this admission his heart and lungs were normal, both on physical and x-ray examination. At this time the specific gravity of his urine never exceeded 1.002. A PSP test showed 75% of dye excreted in two hours. Blood counts were normal. He was placed on pitressin therapy, which successfully controlled his fluid output during the ensuing year. In July, 1947, he was examined at a large clinic, where the first skull films were secured. These were found to be negative. His medication was adjusted and he was discharged.

The first of numerous and repeated episodes of respiratory symptoms appeared two months later in the form of mild head cold with sore throat nasal discharge, and slight cough. The cough persisted, and for a brief period was productive of mucoid sputum. This was followed by sudden, severe, lancinating pains in the right lower chest, lasting 5 days. A month later he experienced similar pains in the left chest. By November, 1947, distressing dyspnea and malaise were becoming evident.

First Admission:—In December, 1947, because of chest pain, dyspnea and cough. Physical examination:—Bronchial breathing and coarse

rales at the base of the left lung. Roentgenograms showed a cyst-like fibrotic process in both lower lobes. White count, 7300 with 83% polys. Sed. rate, 35mm. in one hour (Westergren). The EKG showed no deviation from normal. Sputum and gastric washings negative for T.B.

Patient was transferred to a VA hospital during his second hospital week. Cough was then minimal but the temperature mounted several times to 103F. It was discovered that there had been a weight loss of 17 lbs. in the preceding 8 months. Scattered over the scalp were a number of hemorrhagic, ulcerating lesions measuring from 1 to 3 mm. in diameter. At the lung bases were dullness to percussion, absent to diminished breath sounds, and decreased fremitus. The vital capacity was 1.2 liters (normal 4.3), and chest films showed interstitial fibrosis in both lower lobes and the right middle lobe. Roentgenograms of the skull were negative. The white cell count was now 11,900 with 72% polys. Sed rate was 28 mm. in one hour. The cold agglutination test was negative. Three gastric washings were negative for acid fast bacilli. From the left chest, 200 cc. of bloody fluid were removed, containing numerous neutrophils, but negative bacteria and fungi. Bronchoscopy showed reddening of the bronchial mucosa, but aspirated secretations, when cultured on diverse media and studied by Gram, Papanicolaou, and acid-fast stains, were negative. Thoracotomy was refused by the patient. Before discharge on ec. 2, 1947, an unsuccessful diagnostic attempt to discontinue pitressin was made.

The patient returned to work as a clerk and was troubled only by a mild cough until February, 1948, when he was readmitted for a brief period to the VA hospital because of severe dyspnea. His vital capacity on this admission was unimproved. A right bronchogram showed good filling and some displacement of the middle and lower lobe bronchi, and no bronchiectasis. Only in the upper lobe did the oil enter the alveoli. (This displacement of bronchi seems to be away from lung periphery and toward the mediastinum: don't try to make a diagnosis on this finding. WWV).

Continuing moderate cough and dyspnea with a sudden attack of violent coughing and right chest pain caused him to enter a third hospital in November, 1948. At this time he appeared chronically ill. He had tachycardia, and his temperature was 99° to 101°. On the forehead

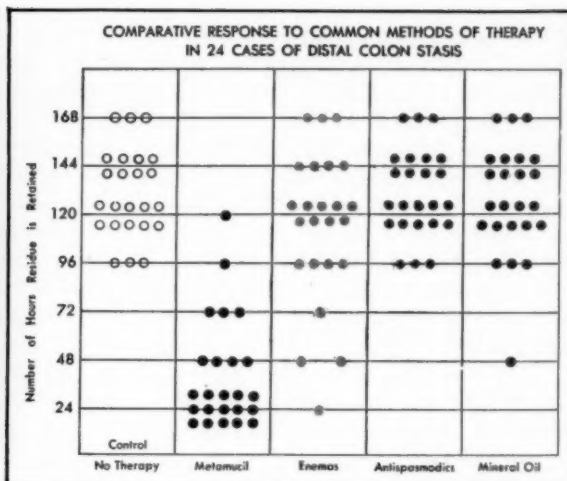
and chest were several small, scarred and pustular lesions. The right tympanic membrane was retracted and covered by purulent exudate. From this exudate *B. proteus* and *E. coli* were cultured. There were moist rales at each lung base and decreased breath sounds at the right base. Chest films were interpreted as indicating idiopathic pulmonary fibrosis with diffuse emphysematous bullae and partial right pneumothorax. Roentgenograms of the skull and bones of the hands were negative. WBC was 10,500 with 84% polys. Serum protein was 7.8 gm, with a reversed A/G ratio of 3.8/4.0. Complement fixation and precipitation tests for coccidioidomycosis and histoplasmosis were negative. Tissue taken for biopsy from one of the skin lesions showed many mononuclear phagocytes and a few round cells not characteristic of any specific disease. The pathologic diagnosis was chronic dermatitis. The patient was treated symptomatically. There was some improvement with 50 per cent absorption of the pneumothorax in two weeks. The 7th and last hospital admission was at this Hospital on Dec. 31, 1948. The patient was in extremis, with a temp. of 102.8, pulse of 120, and resp. rate of 64. There were coarse inspiratory rales throughout both lung fields, but heart sounds were of good quality. The Hgb. determinations showed 11 gm. per 100 cc. and the WBC was 12,500. A few red blood cells and pus cells in the urine. Fever continued, respirations grew more labored, coma intervened, and he expired on January 2, 1949.

#### DR. LOUIS B. BALDWIN

In my meagre experience at hunting birds, I have found that, when shooting with a double barrelled gun, it is advisable to fire at each one separately. So that is what I propose doing with the following two cases.

The first is that of a twenty-three month old Portuguese-American girl, who lived for four months after her admission to the hospital. She had an enlarged liver, jaundice, an elevated blood sugar and slightly elevated blood cholesterol. X-rays of the bones were negative, but those of the lungs showed a moderate amount of diffuse, fine mottled peribronchial infiltration, with a rapid evolution of the pulmonary changes. She ran a low grade intermittent fever and ventually the spleen became palpable. She died following an exploratory laparotomy.

Lymph node, sputum, and skin tests studies



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**SEARLE** *Research in the Service of Medicine*

\*Barowsky, H.: A Roentgenographic Evaluation of the Common Measures Employed in the Treatment of Colonic Stasis. *Rev. Gastroenterol.* 19:154 (Feb.) 1952.

seemed to rule out tuberculosis and fungus infection.

In this infant we have a disease involving primarily the liver and lungs with a rapid progressive course. We assume that the liver pathology and that of the lungs occurred at the same time, because, when she was admitted to the hospital there was apparently not enough pulmonary fibrosis to produce right sided heart failure with cor pulmonale which may occur after extensive pulmonary fibrosis, and which may result in enlargement of the liver and even jaundice. It is extremely unlikely therefore that this infant had bronchiolitis fibrosa obliterans. This is a severe, often fatal disease, characterized by widespread destructive lesions in the smaller bronchioles, followed by a rapidly progressive fibrosis. This disease may be produced by the inhalation of chemical irritants or may follow acute infectious diseases. Berylliosis probably can be classed with this general type of pulmonary condition.

We may also probably correctly assume that tuberculosis and the fungus diseases have been ruled out by the sputum studies and skin tests.

Cystic fibrosis of the pancreas must always be considered in an infant with abdominal symptoms and diffuse advancing pulmonary disease. But in these infants there are the characteristic, loose bulky stools and attacks of vomiting. The blood invariably shows a low cholesterol and a normal sugar.

Medullary neuroblastomas may occur in infancy and young adults, and although the metastasis occur early and may involve the liver and lungs there is usual involvement of the orbit and of the bones.

The next group of diseases to be seriously considered are the so called "lipoidosis" or the disturbances of the reticulo-endothelial system. There is no more intricate or bizarre chapter in medicine than that dealing with these conditions. To understand them one should have a basic knowledge of the physiology and chemistry of lipid substances.

Among the lipoidosis there is the hypercholesterimic xanthomatosis with an elevated total blood cholesterol. For various reasons this condition does not apply to our case.

Then there is the normocholesterimic xanthomatosis; to this group belongs the Schuller-Christian syndrome, in which there are characteristically defects in the membranous bones,

exophthalmos, and diabetes insipidus. The newer concept of this disease recognizes the pathological process as well as the multiplicity of symptoms making it preferable to use a descriptive term. It is now generally referred to as "eosinophilic xanthomatous granuloma." Through the histological studies of Holm, Teilum and Christiansen, it was demonstrated that the natural history of an eosinophilic granuloma comprises four phases:

1. A proliferative phase with accumulation of eosinophilic leukocytes.
2. A granulomatous phase.
3. A xanthomatous phase with nests and isolated foam cells.
4. A fibrous phase.

The generalized form of eosinophilic xanthomatous granuloma characteristically shows brain involvement with diabetes insipidus and exophthalmos, but in the generalized infantile form these symptoms are not reported and there may also be none of the bone changes, so that although early changes may be present they may only be demonstrated by histological examination at autopsy. Skin xanthoma of the "disseminata" type are often noted even in infants but may be absent. Early in the course of this disease the infant develops a cough and bronchitis, which are followed later by fever and signs of lung infiltration. There is marked shortness of breath and there may be cyanosis. The signs of circulatory failure become increasingly prominent and results in death. The lungs show chronic pulmonary fibrosis and diffuse bilateral fibrosis is revealed by x-ray. In some places the lung has a mottled appearance, resembling that in miliary tuberculosis. The superficial lymph nodes are often enlarged but may not show the characteristic foam cells upon histological study.

The liver and spleen were involved in 8 to 26 cases of Schuller-Christian syndrome mentioned by Rowland. In 7 of these cases the enlargement of these organs was never outstanding and even doubtful. Jaundice is not found in cases of the generalized form of eosinophilic granuloma even when the liver is enlarged, because the lesions are only scattered through the liver without causing destruction of the organ structure or producing biliary cirrhosis.

In some cases the only organs involved may be the lymph nodes, liver, spleen and lungs without involvement of the skin and bones. Since these cases exhibit normal cholesterol values, only



chemical analysis and biopsy of the organs can reveal the diagnosis.

Gaucher's disease, also known as reticular and histiocytic cerebrosidosis is another one of the lipoidosis. But this infant does not have the symptoms characteristic of Gaucher's disease, in which, among other things there is a markedly enlarged spleen preceding enlargement of the liver.

Niemann-Pick disease or "reticular and histiocytic splenomyelinosis" must be considered in this infant for it is characterized by enlargement of the liver and spleen, and in the later stages by fever simulating infectious disease and extensive lung involvement, the x-ray of which is very similar to that of miliary tuberculosis. There is no increase in the blood cholesterol in this disease.

With this brief review of the lipoidosis that may apply to our case, it may be seen that none of them explain all the symptoms observed in this infant. However, the rapid course of the disease and the symptoms seem to be explained more readily by the generalized form of eosinophilic xanthomatous granuloma than by any of the other lipoidosis. It is to be noted that there have been atypical case of xanthomatous granuloma reported with jaundice.

The second case seems to have only one common denominator with the first one. They both showed extensive pulmonary pathology with marked pulmonary fibrosis. In the second case there developed a left hemothorax and partial right pneumothorax. In both these cases the changes in the lung progressed rapidly once they were demonstrable by x-ray studies. The second patient was 30 years old when he first showed symptoms of diabetes insipidus. But for four years previously he had a chronic discharging right ear and had a scalp disorder diagnosed as seborrheic dermatitis.

The chest x-ray was negative a few months after the onset of the diabetes insipidus and skull x-rays were negative over a year later. Seventeen months after the advent of polyuria and polydipsia he began having repeated episodes of respiratory symptoms in the form of mild head colds with sore throat, nasal discharge and slight cough. He also contracted pains first in one side of his chest then the other and become markedly dyspneic. Careful studies for tubercle bacilli and fungi were negative.

The obvious question is whether or not we

can combine the skin condition, diabetes insipidus, and pulmonary pathology to represent a disease entity.

Can we be dealing with an example of eosinophilic xanthomatous granuloma? It is now well substantiated by many examples that in this disease there may be diabetes insipidus with pulmonary fibrosis alone or in combination with the dermatitis characteristic of xanthomatosis or any other symptoms such as the bone changes. It is to be noted that the skin lesions do not always show the characteristic lipid containing xanthoma cells. There are, however, two points against the choice of this diagnosis. In the first place it would be unusual for no characteristic yellowish xanthomas to develop if this were a case of xanthomatosis, and in the second place the serum globulin is not increased in xanthomatosis. The normal serum Albumen is 4-5.2 mg. and the globulin is 1.3 to 2.7. In this case the Albumen is slightly depressed and the globulin is increased to practically double the normal figure with a reversed a/g ratio. The diseases in which the serum globulin is increased are the following: Multiple myeloma, pneumonia, active tuberculosis, subacute bacterial endocarditis, rheumatoid arthritis, osteomyelitis, pulmonary abscess, lymphogranuloma inguinale, Kala-azar, Malaria, filariasis, schistosomiasis, leprosy, syphilis, sarcoid of Boeck the leukemias. It may be argued that in addition to xanthochromatosis this patient may have pneumonia or a pulmonary abscess to account for the increased serum globulin.

But we should be remiss if we did not consider the diagnostic possibility of sarcoidosis.

In the comprehensive monograph of Longcope he notes that sarcoidosis may be encountered at any age but usually first appears in young people between the ages of 20 and 40. Neither the aged nor the very young are exempt, for one of the reported cases was 80 years of age, while very young children are reported to have had the disease. The onset of sarcoidosis is generally so insidious that it may only be discovered in the course of a routine examination. There is commonly involvement of the lymph nodes, the skin, the lungs, but almost any organ or tissue may be involved. The disease may extend to the nasopharynx and the paranasal sinuses and penetrate the cribriform plate to the base of the brain. Invasion of the pituitary

gland its stalk or the hypothalamus has occurred early with the occurrence of diabetes insipidus. There is often wide spread involvement of the lungs and pleural effusions or spontaneous pneumothorax have been reported. Although with lung involvement there may be a rapid fatal course in sarcoidosis, the usual story is of remission or healing even when the pulmonary lesions are apparently far advanced.

The disease may have a protracted course with periods of exacerbation or in many instances there may be a spontaneous recovery. Pulmonary tuberculosis is a complicating factor in about 15 percent of the cases and may be the cause of death. The so called seborrheic dermatitis described in this patient is not characteristic of sarcoidosis, nor were later scarred and pustular lesions of the forehead and chest. Boeck originally described three forms of eruptions:

1. The first variety consists of small, firm nodules of waxy aspect with brown or bluish centers.
2. The second variety consists of large nodules, elevated above the surface.
3. The third type is deep seated and the surface is often covered with shiny white scales.

It is interesting to note that cutaneous lesions occur in only 50 percent of the cases. If the skin lesions in the patient under discussion were due to sarcoid, microscopic section should have revealed the typical collection of epithelial cells arranged as tubercles with giant cells, and surrounded by lymphoid infiltration.

What is my diagnosis after this discussion of various possibilities?

1. In favor of xanthomatous granuloma are the age of the first case, and the fact that in adults there may be a combination of Diabetes Insipidus and extensive lung fibrosis without any other symptoms. But in the discussion certain inconsistencies were revealed, nevertheless, this is my diagnosis.

2. In favor of Sarcoidosis in the second case, is the high serum globulin and the occurrence of spontaneous pneumothorax, and pleural effusion, but against it is the fact that although sarcoidosis has been reported in early childhood, I have been unable to unearth a single case in infancy. The symptoms described in the infant, on the other hand, are not inconsistent with those found in sarcoidosis.

#### CASE NO. 1 — 1952-53 DISCUSSIONS DIFFERENTIAL DIAGNOSIS

Dr. Harry L. Mueller: We might pause for a moment to remark that this is a Portuguese infant and that the onset of the jaundice may therefore have been at an earlier date than was suspected, because these children are rather apt to have dark, olive skins.

This patient was in the hospital for four months. If she had a progressive constitutional disease, it is surprising that her condition did not become much worse during that period than is apparent from this history.

Painless, persistent jaundice, with clay-colored stools, and a large liver persisting for four months in a two-year-old infant certainly makes me believe that there was some unusual cause of obstruction to the biliary drainage system. The fact that the child exhibited no gastrointestinal symptoms at an age when almost any disease is accompanied by such symptoms makes me quite confident that there was no disease in the g.i. tract. I am ruling out catarrhal jaundice, which is the common cause of jaundice in a child, although quite rare at this age, because of the long course and the fact that there were no g.i. symptoms.

We must assume a point of obstruction and select the most likely point and cause for that obstruction. I should consider the portal fissure the most likely position and it appeals to me to place Hodgkin's disease in that region. The loss of weight, fever, pulmonary lesions and apparently normal blood picture, as well as the later development of splenic enlargement, are all consistent with Hodgkin's disease. This condition may present an apparently normal blood picture, occasionally has a leucocytosis and may have a relative lymphocytosis, which might explain why the differential count appeared normal, although there was a leucocytosis. The negative biopsy does not to my mind rule out Hodgkin's disease. Another lesion that should be given serious consideration is lymphosarcoma in the same region, although the course of the disease does not fit in so well. Lymphosarcoma is prone to metastasize to both the bronchial and the mediastinal lymph nodes and such metastasis must be considered. Tuberculosis in this position does not often cause pressure symptoms, and with a negative tuberculin reaction and the lack of any report of calcification I should be inclined to rule that out. We might stop here

and get an interpretation of the x-ray films.

Dr. Aubrey O. Hampton: This is a very unusual pulmonary picture. In the first examination it looks very much like miliary tuberculosis. In fact, that would be my unhesitating opinion if I saw this film alone. I should think that it was in the terminal stage and that the patient would die much sooner than in three months — in fact, three days would be more likely. However, the pulmonary picture changes markedly in three months and shifts into something entirely different. At first, there was a miliary process in the lung, and at the last examination there is what appears to be pulmonary fibrosis with emphysema. I have not seen pulmonary fibrosis that started out as a miliary process. In some respects, the progression is like silicosis, which can begin with miliary lesions, and later shifts into extreme fibrosis with blebs, but a child does not have silicosis. The marked increase in the anteroposterior diameter of the chest is like emphysema. Here is the shadow of what appears to be the liver. It is unusually distinct in the lateral view, and not so distinct in the anteroposterior view, but is certainly enlarged. I think that the spleen is moderately enlarged. That film was taken four months before death.

Dr. Mueller: Can you make out any kidney shadows?

Dr. Hampton: The right kidney appears normal in size and shape. I do not see the left.

Dr. Mueller: Is there any evidence of a retroperitoneal mass?

Dr. Hampton: No; and I do not believe that lymphoma would produce this chest picture unless a great deal of radiation had been given.

Dr. Mueller: Could Hodgkin's disease regress as the result of frequent x-ray and fluoroscopic studies?

Dr. Hampton: This is a very diffuse lesion. All the lobes are involved alike. I do not believe we could produce that picture with radiation if we tried.

Dr. Mueller: Is there any evidence of enlargement or calcification of the mediastinal lymph nodes?

Dr. Hampton: No.

Dr. Mueller: I do not know much more than I did before we started, except that I am a little more confused. I am convinced that this child had an obstructing lesion somewhere in the biliary drainage system. We must try to couple it with the pulmonary process and decide

whether the primary lesion was in the lungs or in the abdomen.

Malignant tumors in infants of this age have a very rapid course, and I do not believe that the child would have been in such good condition at the end of four months if the metastases had been so widely distributed. There is also no evidence of a palpable mass, although that could be tucked up under the liver edge. Stone seems very unlikely, with the other aspects of the case, and of course is rare in a child of this age; I do not believe we have to consider it seriously. Foreign body should always be considered in children. Any foreign body that would obstruct the biliary tract would certainly cause some g.i. symptoms. Parasites should perhaps be more seriously considered than I had thought previously. *Distoma* and *ascaris* can both invade the common duct and intrahepatic ducts, as well as the cystic, and can cause obstruction. I should expect stool examinations to pick up some evidence of that. There is nothing in the record to show that the stool examinations were made with that in mind. One other parasite that ought to be considered is the hydatid cyst. The Portuguese are sheepherders. There is no mention in the record that these people had a sheep dog, but a hydatid cyst impinging on the hepatic duct could give a course similar to this. What type of lesion might result in the lungs from ruptured hydatid cyst, I am frank to say I do not know, but I do not believe that has to be seriously considered. Tumors of the pancreas and g.i. tract and kidney are rather unlikely because they would present other g.i. or g.u. signs and symptoms, none of which were present in the entire course. Wilm's tumor must always be considered in a child and on the right side can cause obstruction of the biliary tract. It metastasizes early, and I doubt whether it can present such a picture as this in the lungs. It also metastasizes to bones, and x-ray films of the long bones were negative. Primary tumor of the liver itself seems unlikely. The liver was smooth; it showed no irregularities, and these tumors grow very rapidly and I believe would present other evidence of cancer in the patient.

Turning to the question of infection, syphilis should be considered. Against it are the negative Hinton and absence of changes in long bones and other stigmas. *Brucella* and fungous infections, which have been quite well ruled out by the clinicians, would not present persis-

tent obstructive jaundice with clay-colored stools for that period. Liver abscess is, I think, a greater possibility than I originally considered. It possibly could be the source of multiple septic foci in the lung. It would be unusual for such foci to become fibrosed as these did, but this is an unusual case and we must consider every possibility. Abscess can run a fairly silent course in the lung itself and be very difficult to diagnose, and sometimes is diagnosed only by its metastatic lesions. Congenital anomalies are always a source of worry to the clinician or pediatrician. Liver cysts, cysts of the biliary ducts and stenosis of the ducts could cause half of this picture but not, I believe, the complicated picture in the lung.

I come back to my original thought, that to make a diagnosis in this case an exploratory laparotomy would probably have been necessary, and whether it was done for that reason I do not know. I should say that this child had obstructive jaundice. I do not know to what the lesions in the lungs are due. I had picked as my first choice Hodgkin's disease, but with this picture in the lungs I tend more to favor infection and should say liver abscess or localized infection in the portal fissure. I should also like to put in a guess, because of the patient's nationality, that there is a possibility of a hydatid cyst.

Dr. Mallory: Dr. Hampton, would you be willing to make a diagnosis?

Dr. Hampton: No; I have not the vaguest idea. I should like to know whether an oil spray was used. It could produce that picture in the lungs.

#### *Clinical Diagnosis*

Biliary cirrhosis, obstructive.

Pulmonary fibrosis, chronic, nonspecific.

#### *Dr. Mueller's Diagnosis*

Obstructive jaundice. Liver abscess?

Hodgkin's disease? Hydatid cyst?

#### *Anatomical Diagnosis*

Hand-Schueller-Christian syndrome, with involvement of liver, lungs, lymph nodes, bone and so forth, causing interstitial emphysema (marked) and obstructive biliary cirrhosis.

#### **PATHOLOGICAL DISCUSSION**

Dr. Sidney Farber: (Assistant professor of pathology, Harvard Medical School; pathologist, Children's Hospital). The clinical diagnosis were obstructive biliary cirrhosis and chronic, non-

specific pulmonary fibrosis. The exact nature of the disease was not understood by the clinicians during the life of the child, and nothing was learned from the clinical studies. As Dr. Mueller pointed out in the clinical history, the child was not malnourished and was really more unhappy than desperately ill throughout most of the course.

At autopsy, a granulomatous process that involved many parts of the body but mainly the lungs, the lymph nodes, the liver and the bone marrow, and also the kidneys, uterus and tongue, was found. There was obstructive biliary cirrhosis secondary in part to pressure on the common duct caused by enlarged lymph nodes and a mass of granulation tissue, and in part to compression of the intrahepatic bile ducts by masses of granulation tissue and granulomatous involvement of the liver parenchyma. A considerable amount of fibrous-tissue replacement of destroyed liver parenchyma was present throughout the liver. The greater amount of obstruction was caused by pressure on the common duct. The extraordinary x-ray picture of the lungs was caused by diffuse destruction of the alveolar walls and infiltration of the interstitial tissues of the lungs by the same type of granulomatous process observed in the extrahepatic lymph nodes and in the liver. Secondary to the destruction of alveolar walls, an escape of air into the interstices of the lung occurred, causing numerous small blebs and pseudocysts widely scattered throughout all lobes of both lungs. Histologically, the granulomatous process in the various parts of the body was characterized by the presence of large mononuclear cells, the cytoplasm containing large or small droplets of lipid or cellular debris, varying degrees of fibrosis and a cellular reaction composed of lymphocytes, occasional plasma cells and, in rare places where necrosis was present, polymorphonuclear leucocytes. The lipid material in the large mononucleated cells stained readily by the scharlach red method, and some of the lipid was definitely doubly refractile.

The exact cause of this granulomatous process is unknown, and no further evidence of etiologic value was obtained from this post-mortem examination. Material from the lung and the liver was injected by a variety of methods into a number of laboratory animals without the production of any lesion. Bacteriologic study of the heart's blood and tissue from the liver and



spleen, by aerobic, anaerobic and partial tension methods revealed no growth. The gross and histologic findings were consistent with what has been described as one variant of the Hand-Schueller-Christian disease, and what some writers have called Letterer-Siwe disease. Some patients with lung changes of the same type as those described here have had, in addition, numerous small skin lesions, which are often mistaken for tuberculides. Some of these patients have had destructive lesions of the skull or other parts of the skeleton. The clinical picture is often obscured by the peculiar localization of the pathologic process. In this patient, the icterus was the most significant part of the clinical picture and is explained by accidental obstruction to the outflow of bile by involvement of the extrahepatic lymph nodes. Some patients have severe destruction of the petrous portion of the temporal bone. After operation, a foul purulent exudate, which may persist for weeks or months, may be found, bacterial infection being of only secondary importance.

A study of material obtained at operation and at autopsy of patients of the type under discussion and from patients with less dramatic visceral involvement, or with lesions limited apparently to the skeleton, has forced me to adopt a working hypothesis that Hand-Schueller-Christian disease and the condition that has come to be known in the last year or two as eosinophilic granuloma of bone or solitary granuloma of bone are all variants of the same disease. Certainly it is generally recognized that the classical Hand-Schueller-Christian triad of exophthalmos, diabetes insipidus and skeletal involvement represents but one manifestation of the basic pathologic process. The disease appears to be a self limiting granuloma. Of greatest consequence in the prognosis is the anatomic localization of the lesions.

A Physician: Are the lesions radiosensitive?

Dr. Farber: Yes; we have not had very much experience, but we have learned that the bone lesions particularly are extraordinarily radiosensitive. At this time, we have a patient on the wards of the Children's Hospital with liver involvement similar to that of the patient under discussion today. The liver is receiving radiation therapy.

A Physician: Why did they operate?

Dr. Farber: The operation was performed in

part to relieve biliary obstruction, if possible, and in part to find out the nature of the pathologic process.

Second Case was reported by Dennis and Rosahn, in *The American Journal of Pathology*, July-August, 1951, pp. 627 ff. in paper entitled "The Primary Reticulo-Endothelial Granulomas" as an atypical instance of Letterer-Siwe's disease.

#### POST-MORTEM EXAMINATION

A necropsy was performed 4 hours after death. There was slight cyanosis of hands and face. On the chest and scalp were several scattered, superficial, papular and ulcerated lesions having a diameter varying from 1 to 3 mm. The lesions on the scalp were confined within the hairline. They were scaly and a few were hemorrhagic. Those on the chest were scarred. There were dense and delicate, shaggy adhesions uniting the pleural surfaces bilaterally. The pleura was dull, markedly thickened, and speckled greywhite with scattered hemorrhagic mottling, particularly over the lower lobes of lungs. There was no free fluid in the peritoneal cavity and the peritoneal surface was glistening.

The right lung weighed 655 gm. and the left lung 660 gm. External palpation revealed many scattered, nodular zones. The cut surface of both lower lobes, the right middle lobe, and the lower portions of the upper lobes presented many small and large, irregular, ramifying and intercommunicating cystic spaces and canals. These varied in diameter from a few millimeters to several centimeters. They were lined by a shiny or dull, grayish white surface, and contained either air or a light muddy-brown fluid. External to the cysts the tissue often was dense and fibrous. Many of the cysts seemed to arise from nodular lesions. Bridging the cysts were intact bronchioles and blood vessels. Attempts to demonstrate a communication between the bronchioles and the cystic spaces, by injecting air or water under pressure into the bronchioles, were unsuccessful. Most of the upper lobe parenchyma was firm and consolidated, the cysts having formed in proximity to the hilum. Small emphysematous blebs were noted on all pleural surfaces, and were most numerous at the apices. The only parenchymal tissue spared by the disease was in the superior margins of the upper lobes. The lumina of the bronchi contained abundant foamy, serous fluid.

No gross changes in heart, except right-sided hypertrophy and dilatation. Spleen was congest-

ed with a taut, thickened capsule. The liver and kidneys were congested. Hilar and adjacent mediastinal lymph nodes were enlarged, soft and discrete. Anterior lobe of pituitary slightly enlarged.

#### MICROSCOPIC EXAMINATION

**Lungs.** The principal change in the lungs was a widespread, infiltrative, cellular proliferation arising from peribronchial and interstitial tissues. The cells extended irregularly in all directions into the surrounding lung parenchyma, completely replacing the latter in large areas of the lower lobes. The process varied from dense, compact, cellular replacement of all alveolar tissue, as seen in the lower lobes, to small groupings of pleomorphic cells scattered between large patches of dilated, ruptured and collapsed alveoli. The infiltrative process extended into the interstitial tissue adjoining the alveolar walls. The cysts were irregular in contour and seemed to be formed from a central breakdown of the denser cell masses. The cyst walls frequently were very wide, and were without a true epithelial lining. Most of the larger cysts were empty, and smooth-walled, as if air-containing. Others had roughened, even ruptured, walls and contained free, large mononuclear cells and neutrophils. Intact bronchial and vascular structures, enclosed by a thin collar of fibrous tissue, occupied some of the cyst cavities which sometimes were in direct continuity with alveolar spaces.

The cellular changes were pleomorphic, but the predominant cell was a large mononuclear histiocyte, measuring up to 30 microns in diameter. The nucleus was large, vesicular, well defined, and generally basophilic. As a rule the nuclei were round or ovoid, but some were notched, twisted, bent or reniform. Nuclear chromatin sometimes was quite distinct, with a definite reticular pattern. In a few sites mitotic figures were detected. The cytoplasm was pale pink, occasionally finely granular, with irregular shape and indefinite margin, and usually with a smaller diameter than that of the nucleus. Frequently the cells were tightly packed in massive sheet-like or nodular aggregations. Characteristic lipid granules and doubly refractile bodies were not seen. Mingled with the histiocytic cells were varying numbers of neutrophils, eosinophils, lymphocytes, and a few giant cells. The last appeared to represent fusion of mononuclear cells, and they frequently contained phagocytized cell fragments. They varied in

size from two to four times that of the average mononuclear cell. Fibroblasts were present in some areas. Although fibrous tissue was found in and around the more advanced lesions, it was seen also to accompany small groups of infiltrating cells.

Denuded mononuclear cells were present within a few alveoli, bronchioles, venules and arterioles. Groups of these cells invaded and successfully penetrated bronchiolar, venous, and arteriolar walls. Generally, the lesions were extremely vascular.

**Hilar Lymph Nodes.** Germinal follicles were reduced in size and number. They were compressed by marked proliferation of the cellular process within the sinusoids. Large mononuclear cells, numerous eosinophiles, histiocytes, and giant cells were evident. The capsules were invaded by the histiocytic cells, and were fused. Generalized swelling and neutrophilic infiltration occurred. **Skin:** Reexamination of the original sections of skin taken for biopsy showed the typical mononuclear cells loosely scattered in the dermis. The heart, pituitary gland, hypothalamus, spleen, kidney, — showed small foci of mononuclear and histiocytic cells.

#### COMMENT AT START OF ARTICLE

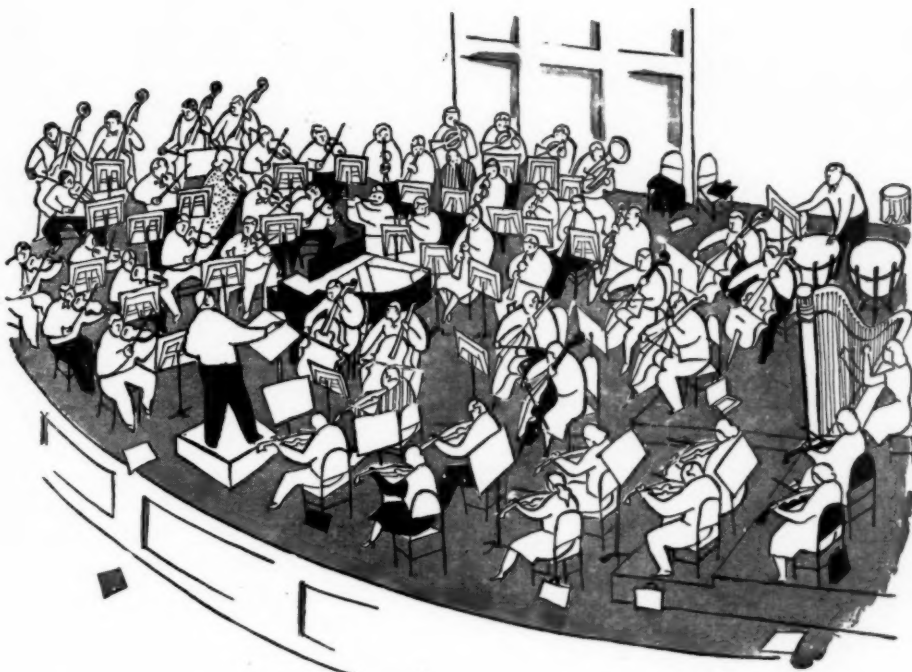
The widened concept of non-lipid reticulo-endotheliosis as a systemic disease with three general expressions has received recognition within recent years. Separation of the Hand-Scheuller-Christian disease from the xanthomatosis was paralleled by the identification of Letterer-Siwe's disease and eosinophilic granuloma of bone. Subsequently, all three were grouped as clinical variants of a basic disorder of the reticulo-endothelial system.

The case reported is believed to be a case of non-lipid reticulo-endothelial granulomatous disease, although not closely corresponding to either of the three variants.

(It was Farber, who discussed the first case) who suggested in 1941 that Christian-Scheuller's disease, Letterer-Siwe's disease, and eosinophilic granuloma of bone were variants of the same basic disease process.

#### DISCUSSION

The case reported here was undiagnosed prior to the patient's death. Only after the histologic sections were reviewed did it become evident that the disease process was related to one of the three reticulo-endothelial disorders. In the past, the general rule has been to consider Letterer-



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Siwe's disease and eosinophilic granuloma of bone as conforming to a limited syndrome, while Christian-Schueller disease has been recognized as having a variable clinical course and anatomical pattern. As a result, the atypical case, especially of Letterer-Siwe's disease, has sometimes been mistaken for Christian-Schueller's disease. Even though the atypical case may not fall clearly into any one of the three microscopic categories, it is the tendency at present to classify a new case on the basis of one of the three following general pictures.

Letterer-Siwe's disease follows an acute and malignant course and occurs predominantly in infants and children. The disease may exist for periods ranging from weeks to several years. There are no foam cells in the lesions save in occasional cases, usually those of extended duration. There is a hemorrhagic tendency. The "Christian-Schueller triad" is rarely seen. Low-grade, continuous fever, moderate to severe secondary anemia, and a moderate leucocytosis or leucopenia appear. Lesions occur almost without fail in spleen, liver, lymph nodes, skeleton, and skin, and occasionally may be found in the lungs, central nervous system, thyroid gland, gastro-intestinal tract and other viscera, and in the thymus, an organ rarely involved by systemic disease. There is no response to treatment and the disease is invariable fatal.

Eosinophilic granuloma of bone has a benign course. The general health remains good. The disease occurs predominantly in infants, children and young adults under 20 years, altho patients up to 58 years old have been recorded. Majority of cases are in males. The duration is brief, though sometimes the process will recur or become chronic. Only rarely are lipid cells seen. Symptoms and signs are meager: some local tenderness, occasional weight loss, variable eosinophilia. Single or multiple bone lesions are present and visceral extension is infrequent. Lesions may develop and heal rapidly. The prognosis is good, as healing of lesions is spontaneous or follows surgical or roentgenological treatment.

Christian-Schueller's disease is a chronic process, with insidious onset, and with extreme variation in course, localization, and clinical manifestations. The patient usually is an adult, although many instances in children are known. Either sex is involved. The disease lasts for many years. Lipoid cells are present at some

time during the course of the disease. Clinical findings depend on the tissues involved, and are not specific, although exophthalmos and pituitary diabetes from bone lesions are frequent. Although the skeleton is the chief system attacked, almost any organ of the body can be damaged directly. The mortality is about 70 per cent. In the very young the disease may have a rapidly fatal course.

The three reticulo-endothelioses are histologically similar with hyperplasia of macrophagic cells and no indication of anaplasia or suppuration. Common to all is the large (15 to 40 microns), pale, polygonal, sometimes round or elongated mononuclear cell, which is present in large numbers and is often phagocytic. The nucleus is large, single, vesicular, oval or indented, sharply outlined, and often excentric. The cytoplasm is pale, dense, homogeneous, eosinophilic usually but occasionally basophilic or neutral and frequently poorly outlined. Small multinucleated giant cells, with four to ten nuclei, sometimes phagocytic, are occasionally present. Reticulum fibers are increased.

Certain histologic features, when present, tend to distinguish the three syndromes. Eosinophilic granuloma of bone is found as a compact tumor enclosed by a fibrous and bony capsule, starting in the medulla and tending to expand and to erode. Letterer-Siwe's disease usually contains discreetly arranged cells in nodular or diffuse formation. Christian-Schueller disease is basically a nodular lesion, and foam cells are intermingled with mononuclear cells, or occur in compact masses. The nuclei may contain lipid droplets, or the cytoplasm, lipid crystals. If proliferative and granulomatous stages only are seen, as in an early lesion, foam cells may be absent and mononuclear cells and eosinophils predominate.

In the case reported the histologic changes have been described. In summary, the predominant cell was a large mononuclear histiocyte with a vesicular basophilic nucleus. Small giant and other inflammatory cells were found. There were areas of necrosis and hemorrhage. The lesions varied from the young proliferative to the older fibrosing type. In places the reticular network was increased and altered. Doubly refractile bodies and foam cells were not found. Lymphoid tissue was reduced. Depending on the organ the lesions had a nodular or diffuse character. In general, the microscopic findings



resembled those noted in the reticulo-endothelial disorders, but they were most like those found in Letterer-Siwe's disease. Yet the distribution of lesions did not conform to the usual picture of that disease.

The organs involved were lung, pituitary body, hypothalamus, skin, heart, kidney and lymph nodes. Pulmonary lesions have been described for all three syndromes, occurring as widespread, interstitial infiltrations. They tend to be fibrotic in Christian-Scheuller's disease, and finely nodular in eosinophilic granuloma of bone. Nodulation is common to all. Emphysema and polycystic pulmonary changes within nodular areas, and spontaneous pneumothorax, are recognized.

The diseases under discussion need to be differentiated from several other disorders. The lesions of Hodgkin's disease, mycosis fungoides, monocytic leukemia, tuberous sclerosis, Boeck's sarcoid, multiple myeloma, xanthoma tuberosum, and other diseases.

The thesis of a fundamental pathologic disorder which is responsible for the three accepted clinical variants and also for the numerous atypical cases which do not follow the prescribed pattern of these variants suggests the advisability of abandoning the present eponymic designations. Instead it is proposed that there be adopted a single all-inclusive term which gives cognizance to the currently unidentified etiologic factor or factors. Such a designation is *primary reticulo-endothelial granuloma*.

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## THE *President's* PAGE

### SCIENTIFIC PROGRAM COMMITTEE

AN ADVANCE OUTLINE OF THE 1954 SCIENTIFIC PROGRAM HAS BEEN FORWARDED TO ME, WHICH REVEALS THAT OUR SCIENTIFIC PROGRAM COMMITTEE HAS BEEN HARD AT PRODUCTIVE WORK. IN DUE COURSE YOU WILL BE INFORMED OF THE FINAL ARRANGEMENT. SYMPOSIA TO BE PRESENTED BY FACULTY MEMBERS OF STANFORD UNIVERSITY, SCHOOL OF MEDICINE AND UNIVERSITY OF WISCONSIN, SCHOOL OF MEDICINE LOOK ATTRACTIVE AND SHOULD HAVE GENERAL APPEAL TO ALL OF US. THE LIST OF GUEST SPEAKERS IS EXCELLENT.

JUST TO REFRESH YOUR MEMORY, THE NEXT ANNUAL MEETING WILL BE HELD AT HOTEL SAN MARCOS IN CHANDLER, APRIL 25 THROUGH 28. THE FIRST SCIENTIFIC SESSION WILL BEGIN AT 10:00 A.M., MONDAY. NOW IS THE TIME TO MARK THESE DATES ON YOUR CALENDAR.

EDWARD M. HAYDEN, M.D., PRESIDENT,  
ARIZONA MEDICAL ASSOCIATION, INC.

# Editorial

## ARIZONA MEDICINE

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The Editor sincerely solicits contributions of scientific articles for publication in ARIZONA MEDICINE. All such contributions are greatly appreciated. All will be given equal consideration.

Certain general rules must be followed, however, and the Editor therefore respectfully submits the following suggestions to authors and contributors:

1. Follow the general rules of good English, especially with regard to construction, diction, spelling, and punctuation.
  2. Be guided by the general rules of medical writing as followed by the JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. (See MEDICAL WRITING by Morris Fishbein.)
  3. Be brief, even while being thorough and complete. Avoid unnecessary words. Try to limit the article to 1500 words.
  4. Read and re-read the manuscript several times to correct it, especially for spelling and punctuation.
  5. Submit manuscript typewritten and double-spaced.
  6. Articles for publication should have been read before a controversial body, e.g., a hospital staff meeting, or a county medical society meeting.
- The Editor is always ready, willing, and happy to help in any way possible.

## THE PHYSICIAN AND HIS INVESTMENTS

IN THE past few years much has been said and written about medical fees. Similarly considerable discussion has been devoted to the high ideals of the medical profession which among other things require the physician to look upon his work as a service to mankind rather than as a means to wealth. The increasing costs of medical care have been a concern to patient and physician alike and the present level of professional fees are justified by the statement that the physician is entitled to live decently, educate his children, and provide for the future

care of his family and possibly himself.

Whether one accepts this philosophy or not most physicians will agree that under present circumstances and with even what should be an adequate income that it is extremely difficult to make an adequate provision for the future. It should be apparent that what funds are available for saving should be invested with great care. Individuals are so at the mercy of broad economic trends beyond their control that there are dangers in any type of investment whether from the standpoint of inherent worth or cheapening of the dollar. Nevertheless there are certain investments which are acceptable and basically conservative in character which except for some catastrophe should make it possible for the physician with a well thought out program and who saves regularly to accumulate an adequate estate. Examples of these are home ownership, insurance, first mortgages on good property, and mutual funds.

The continuing spectacle of professional people investing substantial sums in highly speculative ventures is extremely disturbing and not in keeping with the idealism previously stated. The fact that it is a recognized and long established characteristic of the profession makes it no more wise or acceptable. Equally disturbing is the fact that rather frequently young physicians are making such investments upon the advice or with the knowledge of older and presumably wiser members of the profession.

A rather delicate point also exists in connection with the propriety of the physician accepting managerial responsibilities in connection with business activities outside his profession. There can certainly be no criticism in Board of Director membership with financial or other institutions of impeccable character if the physician's training and aptitude are such that he can play a useful role in such an assignment. He should however carefully avoid relationships in which he exists as a figurehead perhaps to lend an appearance of respectability to ventures of doubtful moral value. He must doubly guard against situations in which his name is used with or without his knowledge in connection with the sale of securities to brother physicians or the general public.

### LETTER TO THE EDITOR

**I**N MY capacity as recently-appointed Acting Director of The Arizona State Hospital, I believe that it is part of my function to inform the medical profession of the plans and programs of the hospital which should be of interest to them.

As the result of a recent meeting between the Arizona State Medical Association Advisory Committee to the Arizona State Hospital (consisting of E. A. Born, Chairman; John R. Green, Lindsay Beaton, Richard Duisberg, and William B. McGrath) and the Hospital Board of Control, the following letter was sent to the Judge and Clerk of the Superior Court of each County:

The Arizona State Medical Association Advisory Committee to the Arizona State Hospital recently met with our Board of Control. The meeting afforded excellent interchange of ideas and was productive of practical suggestions, included among which was the recommendation that we change our present manner of reporting discharges to the committing Court.

In the future, instead of the usual monthly report in which we have aggregated all patients discharged during the previous month, we shall send an immediate report as of the day of discharge to enable the committing Court (and the physician) to afford better follow-up than was possible under the previous system.

A further suggestion was made that a much better out-patient result could be obtained if the Court would then notify either the physician who had served at the time of the commitment, or the family physician who might be responsible for follow-up care. The physician who will care for the patient after his discharge from the hospital can obtain complete information by contacting the hospital directly. In this way they will receive a complete report and a summary of treatment and suggestions for after care.

We are adopting in January 1954 the enclosed form which will be sent you in triplicate to facilitate notifying the appropriate physician,

Cordially,

It has since been suggested that delay might be avoided if the discharge diagnosis were included in the foregoing letter. Consideration had been given to that point and also the inclusion of more detailed clinical information, but it was the opinion of the Hospital staff that in preservation of the confidential relationship which must exist as between doctor and patient,

it would be better to make the foregoing information available only upon application of an authorized physician.

It is hoped that periodic conferences with the Advisory Committee may become a regular thing for we are certain that the results will be beneficial to all concerned. In the instance cited above, we anticipate being able to afford much better service to the family physician, and through him to the patient. This is a very tangible outcome of just one meeting between the Arizona Medical Association and the State Hospital.

The policy of the Hospital staff is to promote the attitude that the Hospital is a place for treatment, not merely a place to keep mentally ill people. Under this program, we begin our discharge planning at the time of the patient's admission. One result is to maintain the contact and interest of the relatives. We shall appreciate any suggestions which will forward this policy and promote its recognition by the public via the medical profession.

SAMUEL WICK, M.D.  
Acting Director  
Arizona State Hospital

### MEETING NOTICES

#### 20th ANNUAL MEETING, AMERICAN COLLEGE OF CHEST PHYSICIANS

June 17-20, 1954

San Francisco, California

#### THIRD INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST

October 4-8, 1954 — Barcelona, Spain

#### SEVENTH ANNUAL POSTGRADUATE COURSE ON

#### DISEASES OF THE CHEST

March 15-19, 1954

Philadelphia, Pennsylvania

### AMERICAN GOITER ASSOCIATION

**T**HE 1954 meeting of the American Goiter Association will be held at the Somerset Hotel, Boston, Massachusetts, April 29, 30 and May 1, 1954.

The program for the three day meeting will consist of papers and discussions dealing with the physiology and diseases of the thyroid gland.



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# TOPICS OF *Current Medical* INTEREST

## RX., DX., AND DRS.

By GUILLERMO OSLER, M.D.

**T**HIS paragraph is a Horrible Example derived from two items in the December issue of ARIZONA MEDICINE . . . The editorial in that number asked "How Much Can One Believe?" about NEW METHODS AND MEDICATIONS, and warned everyone to go slow, take it easy, relax, and be sure of the facts . . . In the same issue, old cautious Guillermo Osler reported a scoop on a new San Francisco drug called 'Gathalone', a form of isoniazid. The preliminary results were terrific . . . Already the usual flaws appear. Perhaps it is simply INH in a form which can be better tolerated. Quite possibly (Los Angeles people say) there IS cross-resistance, so that it would be of no use when sensitivity to INH is gone . . . Some days you can't believe a thing. We'll keep you posted, and warned (and be even more careful).

The use of COMPOUND F in ointment form is an intriguing therapy. It controls edema and erythema, arrests pruritis in some very tough dermic entities . . . Maybe by the time they synthesize it, and we can afford it ('Cortef' of Upjohn's is in tiny tubes at high price), we will know more about its limitations. All hormonal preparations are somewhat like TNT, and ointments are the same.

Many members of the American drinking public have gone over-board for "gin and tonic", a beverage long favored by British colonials, and composed of gin plus a quinine-containing charged water . . . A letter to the J.A.M.A. has recently described an unexpected hazard from this form of imbibing. The drink may protect you from malaria (especially with the incidence as it is in Phoenix and Tucson), but it may let you in for CINCHONISM . . . A case has been described in a man who drank several pints per day, with quinine at the rate of 30 mg., per pint . . . If your ears ring it may not be 'a friend talking about you', it may merely be time to change to Tom Collinses.

'MINNESOTA MEDICINE' published a wonderful retrospective issue last year on the occasion of the state's hundredth year of organized medicine. They had fifteen articles on medical progress, medical schools, surgery, obstetrics, and stories about whatever part of a century the various subspecialties have existed . . . They were real proud, and should be.

Five years ago ARIZONA MEDICINE published a unique symposium on 'Small Desert Animals', as one of its 'Case-Analysis' series. The various

bites, stings, diagnosis, and therapy were all described . . . It was thereafter suggested here that a booklet or series of cards be published with the scorpion, et al, on one side of the page and medical data on the other side . . . Who would do it? It wouldn't be good advertising, it wouldn't pay, etc., etc. . . Have you seen the most recent Disney motion picture sensation? Nothing but the same thing (tho no medical data), and called "THE LIVING DESERT". The advertising is there, and one gets you five that Disney won't lose a nickle.

A small discovery, no bigger than a man's hand, has risen on the scientific sky. It may mean something larger in the future years . . . Coons, Leduc and Connolly have reported that the source of ANTIBODIES is the PLASMA CELL. In rabbits, guinea pigs and mice the site of formation is in the spleen and lymph nodes . . . This gives a function to the obscure plasma cells, and it gives a hope that we may learn more fundamental facts about bodily resistance.

The name has been officialized, so that if you hear of 'VINACTANE SULFATE' it still will mean viomycin (or viomycin sulfate Ciba) . . . The drug is made by several companies, and originally came from actinomyces vinaceus. Its use is limited to tuberculosis, and to those cases where an extra or substitute drug is needed . . . The potency is somewhere between that of streptomycin and PAS, and it probably can best be used with another drug. It is slightly more toxic than the SM drugs, with allergies, renal effects, and neurotoxicity to be watched for.

To those who take it for granted that medicine lacks a time-honoured background on the west coast it might (and should) come as a jolt to read of a banquet given by the Los Angeles Orthopedic Hospital Foundation . . . Staff physicians who had served TWENTY YEARS OR MORE were given citations. Thirty-four, repeat 34, such staff members were present and recognized . . . Ancient and honorable, same like Boston and Philadelphia.

The wife of a New England physician, writing in 'Medical Economics', makes two comments which have long seemed logical to us. One of them you can tell to your wife; it might be wise not to tell her the other . . . 1. Contrary to the old saw, the author believes she is LUCKY to be a doctor's wife when she is ill. Families of M.D.'s are NOT neglected; they get good care (but often don't take it) . . . 2. A doctor's wife should be



THE HOSPITAL BENEFIT

# Bulletin

Special

Published Bi-Monthly by the Hospital Benefit Association, First Street at Willetta, Phoenix

February, 1954

## Question Quiz

Do you know the answers?

- Q. When I treat a Member of the Hospital Benefit Association who has Surgical Protection, am I supposed to charge exactly according to the schedule of fees paid by the HBA?**
- A.** No . . . not necessarily. If your charge is under the amount paid by the HBA, you will, of course, receive full payment of your bill. If your charge exceeds the benefits to which the Member is entitled, you will bill the patient for that portion not paid by the HBA.
- Q. Are there any cases where the surgeon charges exactly what the HBA will pay?**
- A.** Yes. Many surgeons, when they learn that the patient is a Member of HBA, charge exactly according to the fee schedule. This way, they can be certain that they will get 100% of the amount they bill. Payment is quick, and the possibility of ever having to pay collection charges on the account is eliminated.
- Q. Just how soon does the HBA pay surgical bills?**
- A.** The check is sent within 3 to 5 days after the claim form is received from the doctor. And here's a situation where the doctors can help themselves. The sooner the claim form is filled in and returned to the Association, the sooner the payment can be made! Send in your claims promptly, and you will be paid promptly.
- Q. Do any Members of the Association have Surgical protection without having a Hospital Plan?**
- A.** No. The Surgical Plan is available only to members who have enrolled in one of the Hospital Plans offered by the Hospital Benefit Association.

## Surgical Fees For Accidents Also Cover After-Care Costs

It has come to the attention of the HBA that many Members have not been receiving full benefits due them under the Surgical Plan. The most frequent cause of this is re-visiting the physician's office after emergency treatment for accident.

Let's use a typical example: a Member accidentally receives a wound that requires debridement, with closure. He rushes to his physician's office for treatment.

The physician bills the HBA \$10, the HBA pays it, and the case closed as far as the Association is concerned.

However, the patient has to make two more visits to have new dressings and the stitches removed. The physician bills the patient \$4 each for these visits, and the patient pays it, never realizing that the HBA would gladly pay. He actually is eligible for benefits totaling \$20 for this type of treatment, including after-care.

The solution to this, as many doctors have found, is to make a claim to the HBA for what you figure the total cost of all the treatments will be, barring complications. If the charge for the first call is \$10, and it looks like two more visits at \$4 each will be needed, you should bill the HBA for \$18.

And always remember: the Association will pay for treatment of accidental injuries in the physician's office, providing the treatment is performed within 24 hours after the accident.

## MEET OUR DIRECTORS



Conrad T. Kleinman

Conrad T. Kleinman, prominent Phoenix attorney, has been a member of the board of directors of the Hospital Benefit Association since 1951. Bishop of the 8th Ward L.D.S., Kleinman is a partner in the law firm of Rawlins, Davis, Christy, Kleinman Burris, the firm that drew up the original incorporation papers for the Association.

### Harvard Law Graduate

Kleinman graduated from the Harvard Law School in 1939. In 1934, he married Lucille Lamour, an Oregon girl who graduated from the University of Arizona. The Kleinmans have two boys, Larry, age 13, and Jan, age 10.



What do you mean. "Good News"? My name is MISS Mary Brown!

more careful in practicing medicine among her friends. Maybe her territory should be confined to one block (or 'square', as they say in the East). Even then she may run into other homestakes! . . . If the Women's Auxiliary reads this, we are only kidding.

An ancient New Hampshire country doctor (84 years of age) gives an odd personal opinion of what the public expects of medical care — Fifty years ago people would think a physician didn't know much if he couldn't cure them in 20 minutes, but now people do not expect the impossible . . . We'd have thought the reverse, what with everyone knowing about new drugs and new methods, or at least hearing about them.

The Wisconsin Anti-Tuberculosis Association makes a small joke while coining a slogan to protect school children. The WATA 'Crusader' changes the saying "An Apple for the Teacher" to "AN X-RAY FOR THE TEACHER" . . . It is odd that any place exists where there isn't an X-Ray for teacher, and regularly too. They could even add a jingle to their saying — "Christmas comes but once a year; so does a film for teacher dear".

Every now and then something in life becomes very complicated or obscure. Even when one does a 'double-take' it still doesn't make sense, and it seems as tho the world has left us behind . . . We have mentioned some of the 'real big' terms used in electronics, but it hardly seemed probable that the Nat'l. TB Ass'n. would give us the jive. They now have an appointed group of six called the "Committee on Definition of Income Subject to Percentage" . . . As my cousin Mortimer Snerd says, "Yup!"

This story concerns THREE DISSIMILAR PHYSICIANS and a recent medical convention (and, possibly, a bit of humor) . . . One of the physicians, since then doing clinical research in Paris, had an exhibit at the convention. It illustrated some of the work he had done to show that the PRESSURES IN A 'PNEUMO' SPACE do NOT vary directly and regularly with the atmospheric pressures outside the body. His tests had been made in elevators and airplanes, which is unusual enough, but his exhibit was an even more wondrous affair, with a juke-box-like machine and a manometer 10 feet high . . . The second physician is a catalyst. He likes to bring people together and observe what happens . . . The third M.D. was a quiet clinician, who, with his father, had once published articles on atmospheric pressures, flying, and pneumothorax. He also has, in a quiet way, a sharp eye and tongue . . . Doctor Number Two took Number Three to the exhibit of Number One where there were a number of observers watching the devices. Dr. One was introduced to Dr. Three and failed to recognize him. He proceeded to start the series of procedures which illustrated his

theses. As one reaction followed the other, and finally the red indicator shot to the top of the huge manometer, Dr. One said, "Well! What do you think of it?" Dr. Three thought for about ten seconds, drew a deep breath, and said, "It sure knocks the devil out of Boyle's Law, doesn't it?"

## TEST YOUR MEDICAL KNOWLEDGE

(This innovation was suggested by Dr. Oatway, and the questions selected by our reviewer. Twelve correct answers would be average, fifteen would be good; eighteen would be super, and twenty correct answers dug out of your own head would mark you as a medical genius. Answers will be found on page 74.)

Ques. 1. What are streptodinas and streptodornase and for what conditions are they used in practice?

Ques. 2. Can you commit suicide by voluntarily holding your breath?

Ques. 3. What is the most fatal complication of polycythemia vera?

Ques. 4. What is the latest reported treatment for the symptoms developing after a bite by *Latrodectus mactans*?

Ques. 5. What limits the value of radioactive iodine in treating thyroid carcinoma?

Ques. 6. When operating upon elderly patients for acute appendicitis, what other important lesion should always be looked for, and why?

Ques. 7. What is the best drug for treating acute gout?

Ques. 8. What is the mechanism of syncope produced by coughing?

Ques. 9. What is the Cold Pressor Test and its diagnostic significance?

Ques. 10. What is the trade name of phen-tolamine and what is it used for?

Ques. 11. Right or wrong. "When most indicated, oral cholecystography is least reliable."

Ques. 12. What is the Hamman-Rich syndrome, and the latest treatment advised for it?

Ques. 13. Name ten conditions which produce solitary circumscribed shadows (lesions) in the lungs.

Ques. 14. At the present time what clinical conditions are grouped under the classification of "collagen" diseases?

Ques. 15. About what is the percentage



incidence of trichinosis in the population of the United States?

Ques. 16. What was the origin of the word "fee"?

Ques. 17. What is the significant difference, aside from the amount of potassium ions, between potassium deficiency and potassium intoxication?

Ques. 18. Who is regarded as the "Founder of Occupational Medicine?"

Ques. 19. What is Tubalex, how administered and for what conditions?

Ques. 20. Is there a consensus of opinion about trauma and cancer in a causative relationship? If so, what is it?

### BOOK REVIEW

DISABILITY EVALUATION, Principles of Treatment of Compensable Injuries by Earl D. McBride, B.S., M.D., F.A.C.S., Assistant Professor in Orthopedic Surgery, University of Oklahoma School of Medicine; Attending Orthopedic Surgeon to St. Anthony's Hospital. Fifth edition, 1953, J. B. Lippincott Company, Price, \$15.00.

THIS fifth edition contains many improvements over the previous editions of this well known standard reference work. The purpose of the volume is well stated in the preface to the first edition and is "To interpret the physiological and mechanical alterations arising out of injury to the motor structures to the human body, and to reasonably appraise and evaluate the extent of functional loss as it relates to the economic incapacity of the injured." This is undoubtedly a volume which should be in every practicing physician's reference library or readily available in some other convenient reference library. Most physicians, regardless of their field of practice, are called upon at some time or another for consultation in some industrial injury case and unless some reference work of this type is available or unless the physician has a wide experience in evaluating industrial dis-

abilities, his estimate of his patient's disability is likely to be more in the nature of an intelligent guess than a scientific evaluation.

The various types of disability, together with the criteria for evaluation of the amount of disability present and with abundant illustrations showing the tests involved are all here and should be invaluable to the physician confronted with a disability problem. The widespread use of this text should lead to sound and consistent disability benefits.

### PAN-PACIFIC SURGICAL ASSOCIATION SIXTH CONGRESS

Honolulu, Hawaii

October 7-18, 1954

DOCTORS are cordially invited to attend the Sixth Congress of the Pan-Pacific Surgical Association to be held in Honolulu, October 7-8, 1954 and are urged to make arrangements as soon as possible if they wish to be assured of adequate facilities.

An outstanding scientific program with over 100 leading surgeons, including sessions in all divisions of surgery and related fields, promises to be of interest to all members of the profession. An extensive social program is being developed for the doctors' families.

The Association office has been appointed as travel agent for those attending the Congress and it is important that all hotel and travel reservations be made through the Honolulu headquarters of the Pan-Pacific Surgical Association.

For Further information, please write to F. J. Pinkerton, M.D., Director General, PAN-PACIFIC SURGICAL ASSOCIATION, Suite Seven, Young Building, Honolulu, Hawaii.

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### ANSWERS TO — TEST YOUR MEDICAL KNOWLEDGE

Ans. 1. Enzymes produced by certain strains of streptococci. They have been used for the liquefaction of purulent and hemorrhagic exudates in closed cavities, in amebic abscess, in unresolved pneumonia, etc. (*New Eng. Journ. of Med.*, Oct. 15, 1953, p. 652.)

Ans. 2. Cases are recorded but the method is not recommended as an easy or certain "way out." (*New Eng. Journ. of Med.*, Oct. 22, 1953, p. 698.)

Ans. 3. Myelogenous leukemia. (*Brooklyn Hosp. Journ.*, Third Quarter, 1953, page 135, *Clinico-Pathological Conference.*)

Ans. 4. This is the black widow spider and the severe pain is due to muscle spasm. Latest treatment recommended for the pain from this spasm is d-tubocurarine chloride. (*Ann. Int. Med.*, Sept. 1953, p. 62.)

Ans. 5. The poor uptake of the iodine by most carcinoma tissue. (Schultz in *Journal Lancet*, Oct. 1953, p. 403.)

Ans. 6. Cancer of the colon because acute appendicitis is a complication in 10 per cent of the cases of colon carcinoma. (*Texas State Journ. of Med.*, 49: 1953, p. 222.)

Ans. 7. There is no improvement over colchicine in acute gout. It is still the stand-by after 100 years. (*Journ. of the Mich. State Med. Soc.*, Sept., 1953, p. 959). (Also Haines in *Southwestern Med.*, Nov., 1953, p. 409.)

Ans. 8. Acute diminution of supply pressure of blood to the brain. (*Brit. Med. Journ.*, Oct. 17, 1953, p. 860.)

Ans. 9. Testing the blood pressure before and after immersing the hand for one minute in ice water. If the B.P. rises more than 20 mm. systolic and 15 mm. diastolic in a hypertensive condition, the suggestion is essential hypertension. If it fails to rise or does not increase more than 20/15 mm., better study the patient for possible pheochromocytoma. (*DeCourcy.—Pheochromocytoma and the General Practitioner*, p. 35).

Ans. 10. Regitine, and it is used as a test for a possible pheochromocytoma. (Emlet et al, *J.A.M.A.*, Aug. 11, 1951, p. 1383).

Ans. 11. Right, because visualization usually fails when this examination is most indicated, — in the differential diagnosis of intrahepatic and extrahepatic obstruction. (*Ann. Int. Med.*, Sept., 1953, Keil, et al, p. 479).

Ans. 12. Diffuse interstitial fibrosis of the lungs. Corticotropin or cortisone reported as effective in abating symptoms, (by Schechter in *Am. Rev. of Tuberculosis*, October, 1953, page 603. See also report of case by Wilson in *The Journ. of the Arkansas Med. Soc.*, Sept. 1953.)

Ans. 13. Pneumonitis, abscess, infarction, hydatid cyst, tuberculoma, coccidioidosis, brucellosis, oil granuloma, adenoma, carcinoma. (See Hodgson and McDonald, *Diseases of Chest*, Sept., 1953, page 289 ff.)

Ans. 14. Systemic lupus erythematosus, rheumatoid arthritis, rheumatic fever, dermatomyositis, periarteritis nodosa, scleroderma; maybe others. (see article by Wells and Ross, *Texas State Journ. of Med.*, Sept., 1953, p. 673.)

Ans. 15. According to one writer, 37 per cent or more. (See article by Kushlan in *Connecticut State Med. Journ.*, Sept., 1953, page 751).

Ans. 16. Meaning payment for professional services, it is derived from the Anglo-Saxon word "feoh" meaning cattle, and goes back to the time before money, when cattle were a means of payment. (*Ohio State Med. Journ.*, Sept., 1953, p. 818).

Ans. 17. In deficiency the symptoms are due to cellular potassium depletion and the serum potassium concentration may be normal. In potassium intoxication, the symptoms are directly related to the extracellular potassium concentration, and not to the cell potassium content. (See article by MacPhee in *British Med. Journ.*, Sept. 5, 1953, p. 528).

Ans. 18. Bernardino Ramazzini (1633-1714), who did his important work at the University of Padua. (See *Industrial Med. & Surg.*, Sept., 1953, p. 403).

Ans. 19. Trade name for d-tubocurarine; put up in pellets for sublingual administration and in suppositories for rectal administration. Used in muscle spasms, associated with a variety of conditions. (see article by Neff and Mayer, *California Medicine*, Sept., 1953, page 227.)

Ans. 20. "The common lay belief that simple mechanical injury — as a blow or contusion — as a carcinogenic factor is denied." (See article by Pedden, in the *Journ. of the Michigan State Med. Soc.*, April, 1953, page 414).



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## ARIZONA *Pharmaceutical* PAGE

### PRESIDENT, AMERICAN PHARMACEUTICAL ASSOCIATION



Newell Stewart

**T**HE PHARMACISTS of Arizona are proud to present to the members of the Arizona Medical Association the Secretary of the Arizona State Board of Pharmacy and of the Arizona Pharmaceutical Association, NEWELL STEWART, who has just been elected President of the American Pharmaceutical Association. Mr. Stewart will be installed into the office of the presidency at the 103rd annual meeting of the Association to be held in Boston, Massachusetts during the week of August 23rd, 1954.

We feel that Mr. Stewart's selection for this office by the pharmacists of America is a distinct honor, not only to him, who deserves it and not only to the pharmacists of our state, but to the many friends amongst the members of our allied professions.

Newell Stewart was born in Sistersville, West Virginia February 14, 1900 and attended elementary schools there. Following high school graduation, he spent two years in the College of Engineering at West Virginia University. He served in World War I and after this service returned to the University of West Virginia where he entered the College of Pharmacy and was graduated therefrom in 1923.

Mr. Stewart came to Arizona in 1925 and has owned retail pharmacies in Arizona from 1926 to 1952. He was appointed to the Arizona Board of Pharmacy in 1936 and served as its secretary in 1937, 1940 and continuously since 1942. He is editor of the Arizona Pharmacist and a past president of the Arizona Pharmaceutical Association and has been secretary of the organization for the past eleven years. In addition to his duties as secretary of the Board and Association, he is a member of the faculty of the College of Pharmacy at the University of Arizona where he teaches Pharmaceutical Jurisprudence. Mr. Stewart also continues to be a practicing pharmacist intensely interested in every phase of retail and hospital pharmacy. He has served as a member of the Board of Memorial Hospital in Phoenix, Arizona for the past nine years and has been solely responsible for the operation of the Memorial Hospital Pharmacy during that time. The Memorial Hospital Pharmacy is a model hospital pharmacy setup and has been copied again and again in hospital pharmacy planning in Arizona.

With his many interests and duties here in Arizona, Newell Stewart has still found time to devote to pharmacy on a national level. He is a past president of the National Association Boards of Pharmacy and served on the Executive Board of this group for three years. He was chairman of the House of Delegates of the American Pharmaceutical Association in 1950-51. He has served on many working committees during the past years in all the national pharmaceutical organizations of which he is a member, including, in addition to the American Pharmaceutical Association and, National Association Boards of Pharmacy, the American College of Apothecaries, the American and Arizona Societies of Hospital Pharmacists; the National Association of Retail Druggists and the National Conference of Pharmaceutical Association Secretaries. He holds membership in Rho Chi, National Honorary Pharmaceutical Fraternity, and Phi Delta Chi, pharmaceutical fraternity.

Mr. Stewart has always taken an active part in civic affairs; he served as Mayor of the City of Phoenix from 1942 to 1944, devoting time to war loan drives and community chest work during the time. He has been an active worker in the Boy Scout organization for many years; is a member of the Masonic order and the Shrine and served as Arizona Deputy Order of De Molay for several years. He has been an active member of the First Baptist Church in Phoenix for many years.



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## Interesting TOPICS

### PROBLEMS OF CANCER OF THE STOMACH

**H**ODGSON and Kirklin, of Mayo Clinic, have one of their always fine, concise, papers in South Dakota Journ. of Medicine and Pharmacy, for January, 1953,—this time on the "Roentgenologic Diagnosis of Carcinoma of the Stomach." The paper is written for general practitioners. A few pertinent quotations will be better than attempt to abstract this paper.

"Gastric carcinoma represents one of the most difficult unsolved problems in medicine today."

"Because of the insidious onset of the disease, the only hope of improving the discouraging situation is in earlier diagnosis . . . best accomplished by close cooperation between clinician and roentgenologist."

"Any patient more than 40 years of age who has even the most minor gastrointestinal symptoms" should have roentgenological examination of the stomach.

"Any neoplasm than can be seen macroscopically can be demonstrated by roentgenologic methods."

They then discuss the types of carcinoma of the stomach and roughly outline the technics of examination with certain pitfalls.

"Operation is the only treatment that offers any promise of cure . . . and the responsibility for early diagnosis must be shared by both clinician and roentgenologist."

W.W.W.

**PEPTIC ULCER.** Medical Progress Review by Zetzel in two issues of The New England Journ. of Med. (June 4 and 11, 1953).

**THE PROGNOSIS IN GASTRIC ULCER TREATED CONSERVATIVELY.** Banks and Zetzel, Ibid, June 11, 1953.

Peptic ulcer is still a subject of prime importance to general practitioners, internists, as well as to surgeons. Two recent comprehensive books have appeared on the subject (Ivy, Grossman and Bachrack's and Sandweiss's) and Zetzel reviews some ninety or more articles on the subject. According to Wangenstein, there is an annual mortality of 10,000 from peptic ulcer, which afflicts from 5 to 10 per cent of the adult

male population in the United States and England. Peptic ulcer is a chronic disease involving the upper gastrointestinal tract (esophagus, stomach and duodenum) in areas exposed to an acid gastric juice. "No acid, no ulcer" is still a valid truism, and the keystone of the current medical practice regarding peptic ulcer. In spite of reports of peptic ulcer with achlorhydria, "the overwhelming weight of evidence establishes the presence of free HCl as the *sine qua non* of ulcer activity. Under drug therapy, this reviewer states: "The ideal drug in ulcer therapy should have the following characteristics; a prolonged neutralizing effect without a secondary or rebound increase in secretion; palatability; capacity to promote healing and prevent or delay the onset of recurrences and complications; effectiveness when taken by mouth; promptness in relief of symptoms; and noninterference with the process of absorption."

He then reviews a number of drugs and medicinal preparations,—such as calcium carbonate, magnesium preparations, aluminum preparations, SCMC, mucin, protein hydrolysates, anion-exchange resins. The anticholinergic drugs reviewed include atropine, banthine, hexamethonium, TEAC, dibuline, prantal and antrenyl, enterogastrone, urogastrone, kutrol, eugenol, antihistamines, chlorophyll, tropine, and ACTH. He reviews the articles on emotions and ulcer, x-ray therapy, hemorrhage, perforation, obstruction and intractability, and a final section on gastric ulcer because of the question of malignant degeneration enters into it.

In the article by this reviewer and Banks (v. supra), they conclude that the prognosis of gastric ulcer under medical treatment is not reassuring, because of the failure to observe rigid clinical and laboratory safeguards. They think the risk of malignant degeneration compares favorably with the operative mortality of resection. "There is need for a wider publicity of the known facts concerning gastric ulcer among the profession and the public."

(NOTE:—This review and this article are well worth the time and trouble of any practitioner who has to deal with the problem of peptic ulcer.)—W.W.W.

# Woman's AUXILIARY

## TODAY'S HEALTH

**E**ACH of the past three years has seen our state increase the number of subscriptions to Today's Health. We placed fourth in the National Contest in 1952-53. This was accomplished not by a few, but by all of the County Auxiliaries. We are now on our way to an even greater increase for 1953-54. However, this increase can only be accomplished if each county auxiliary member feels the responsibility for positive health education and good public relations through subscriptions to Today's Health. Here are a few ideas which may help you do a 100 per cent job.

1. Subscriptions to Doctors: this should be 100 per cent in each county. Definitely an outlet of positive Health education.

2. Subscriptions to Dentists: The same as above. The main idea in both of these is to work. Subscriptions are not obtained from either of these groups or from the lay-public without a hard working committee on Today's Health.

3. Subscriptions to schools: This may be done by contacting the school superintendent or the school nurses or those teachers who are directly responsible for teaching health, also a gift subscription to the P.T.A. President or Health Chairman.

4. Subscriptions through increasing size of sales force, such as visiting local women's clubs, P.T.A. groups, etc. Tell them about Today's Health. Give free copies which may be had by writing the National Office. If your county has a Yearly Fair, plan to give out free copies. By this you are able to acquaint many with

Today's Health, who otherwise would not know what our magazine offers in fine accurate information.

5. Subscriptions for Congressmen and State Legislators. Ask your Medical association legislative chairman to give their representatives a gift subscription. They need to know more about the public health of our State and will pay more attention if given by the Medical Society.

Our main objective is to place positive Health education in the hands of the public through Today's Health.

Mrs. James C. Soderstrom  
Chairman Today's Health  
Whipple, Arizona

## NEWS ITEM

Joseph F. Milan, M.D., Maricopa County Hospital, Phoenix was taken in as a Junior Member of the Maricopa County Medical Society at their Meeting of January 4, 1954.

## MR MEDICAL RENTS

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MEDICINE REACH ITS READERS  
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Material arriving after that date will be published  
the following month.

## PEDIATRIC CLINICS OF NORTH AMERICA

**T**HE odds may be as high as 150 to one against a child contracting polio during the first 20 years of his life, it was estimated in the introductory issue of a new medical publication now being distributed to the nation's physicians.

The publication, entitled *Pediatric Clinics of North America* and containing nine definitive articles on polio, was prepared with the editorial assistance of the National Foundation for Infantile Paralysis. It is published by W. B. Saunders Company of Philadelphia, medical book publishers.

Designed to provide the latest information on the diagnosis and management of polio, the introductory issue is being distributed free of charge by the W. B. Saunders Company to 110,000 practicing physicians in the United States.

The first regular issue is due in February, 1954 and every three months thereafter. The publications will present symposia on methods of management currently in use for the handling of various pediatric problems.

Contained in the symposium are articles by: Dr. David Bodian, Johns Hopkins School of Hygiene and Public Health; Dr. Alex J. Steigman, University of Louisville; Dr. James L. Wilson, University of Michigan School of Medicine; Dr. Jessie Wright, University of Pittsburgh; Dr. William T. Green, Harvard Medical School; Dr. Howard A. Rusk, New York University College of Medicine, and Dr. Jonas Salk, University of Pittsburgh.

## VA To Ask Financial Information In Non-Service Connected Cases

**U**NDER a new policy, Veterans Administration from now on will ask additional information from a veteran applying for hospitalization of a non-service connected condition. Previously, the veteran had only to answer the question: "Are you financially able to pay the necessary expense of hospitalization or domiciliary care?" If the answer was "no," the veteran was eligible. Now the veteran will be required to answer the following additional questions:

1. What is the current value of your property, real and personal?
2. What is the current amount of your ready assets in the form of cash, bank deposits, savings bonds, etc.?
3. If you own real property, what is the approximate amount of the unpaid mortgage or other indebtedness?
- 4.

What are your average monthly expenditures, including mortgage payments and all other personal expenses, including your expenses for dependents? 5. What was your average monthly income for the last six months, from all sources?

However, VA states that, "This addendum may be used in no way whatever to deny hospitalization to a veteran, as the law specifically provides that 'the statement under oath of the applicant . . . shall be accepted as sufficient evidence of inability to defray necessary expenses.' (It) is designed to protect applicants for hospitalization, and veterans generally, from charges of 'chiseling' on the government."

The reader is referred to Circular No. 11 of November 4, 1953 of the Veterans Administration and Form 10-P-10a for more complete and interesting information.—ED.

## MEDICAL LITERATURE NEEDED ST. GEORGE'S MISSION HOSPITAL

Travancore, S. India

Gentlemen,

I wish to inform you that the above Hospital is a non-profit organization situated in a hilly village and working among the poor labour classes of the locality and its suburbs. As good medical literatures are very few in this part of the world, a small library is started recently, attached to the above Hospital with the idea of collecting used medical journals, books, bulletins, Transactions of Medical Societies etc., from all available sources in foreign countries so that up-to-date knowledge in medical practice may be obtained.

Further Ayurvedic and Unani systems of Medicine are very troublesome competitors to Allopathic system here and proper equipments and medical literatures are highly essential for the successful management of the Hospital.

In the light of the above circumstances, I request you to kindly issue a News Note in your monthly Bulletin and also in your Association Medical Journal requesting the sympathetic members of your Association to send me their used medical journals with all available backward copies, Medical books, reprints of articles and other useful Medical literatures along with secondhand surgical instruments, Medical appliances, Laboratory equipments etc. and gift parcels containing antibiotics, liver extracts and other patent medicines so that many of our poor patients may directly and indirectly be



benefitted by them.

This act of kindness and charity by the members of your association will ever be remembered and lapse of time cannot wipe away from our memory.

Thanking you very much for all your valuable services,

Yours Very Truly,  
DR. T. K. THOMAS  
Hon. Medical Superintendent

ST. GEORGE'S MISSION HOSPITAL  
Punalur, P. O., Travancore, S. India

*True copy of the requisition for X-Ray Literatures published in the American X-Ray Technician dated March, '53.*

#### BOOKS FOR INDIA

A letter has been received from a Doctor in a Mission Hospital in India, requesting good radiological books, Journals et cetera. The doctor states that very few books are available at the hospital. The few books that are for sale are very expensive and the hospital is unable to pay for them. This institution is a charitable one and theirs funds are very limited.

The X-Ray Technician will be sent to the hospital regularly with compliments of the ASXT.

Members of the ASXT are requested to send books on radiography and medicine, that are still up to date, but are not being used. Old copies of medical journals will be acceptable.

Address all material to Dr. T. K. Thomas, Medical Superintendent, St. George's Mission Hospital, Punalur P.O., Travancore, S. India.

*Copy of the News Note published in the Journal of the Christian Medical Society of U.S.A. dated November - December, 1952.*

#### SPECIALIST NEEDS LITERATURE

I am interested in Radiology, Dentistry and in diseases of Eye, Ear, Nose & Throat. If some of the members care to send me some literature concerning the above specialties, it will be a source of great help in my profession. I am trained in the above specialties in the American Presbyterian Hospital, Miraj, India, and I wish to inform you that I am the only specialist in the above subjects in this locality for nearly two lakhs of population. This locality is very famous for its Bolshevik activities, and I have a lot of work to do other than professional. Recently we have formed a new Association to start work against Bolshevik activities. A few months back I received a few copies of the

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J. A. M. A. from a member of the C. M. S., Dr. William Johns and indeed it was a great help to me. I am extremely thankful to you for all your help and I earnestly pray for the society as well as for all its members.

DR. T. K. THOMAS,  
St. George's Mission Hospital,  
Punalur P. O., Travancore, S. India.

#### HOW DO YOU PRACTICE MEDICINE?

**M**ALPRACTICE suits are usually the results of the failure of a physician to perform his duty properly. The establishment of a suit depends upon the proof, (1) that the physician failed to do his duty, and (2) that as a result, injury to the patient resulted.

A physician has an implied contract with his patient to render services. This implies that the physician has reasonable skill and will apply this skill in the treatment of the patient. From a legal standpoint the physician implies in his acceptance of the patient's care, that he possesses and will exercise that reasonable and ordinary degree of skill and learning which has been established by his fellow practitioners in the same or like communities.

Physicians may:

- (1) Apply bad, wrong, or injudicious care from
  - (a) Ignorance
  - (b) Carelessness
  - (c) Want of proper professional skill
  - (d) Disregard of established rules or principles
  - (e) Neglect

Any one of which may cause in the patient

- (a) Injury
- (b) Unnecessary suffering
- (c) Death

Most malpractice suits would fit into the above diagram. To illustrate some of the various ramifications covered in the physician's legal duties, the following are taken from Regan's book, "The Doctor and the Patient and the Law".

- (1) The physician must not neglect or abandon his patient.
- (2) He must give his patient sufficient attention.
- (3) He must not experiment.
- (4) He must proceed diligently without unnecessary delay.

(5) He must follow good practice, common practice in diagnosis, and treatment.

(6) He must find or anticipate any condition reasonably determinable or reasonably likely to develop.

(7) He must utilize diagnostic aids.

(8) He must obtain legal consent to operate and for autopsy.

(9) He must give proper instructions for the care of the patient and for the protection of those coming in contact with the patient.

(10) He must fulfill the terms of a special contract if he makes one.

Your patient is important — to himself and to you. (Utah Medical Bulletin)

### MEMBERSHIP REPORT

Membership of the State Association on January 1, 1954 totalled 723, representing a net gain of 42 since January 1, 1953. During the past year 72 physicians were admitted as new members; 2 were reinstated; 15 moved from the state; 7 were dropped; 3 resigned; 7 were deceased.

Included in the 723 membership total are 675 Active members and 48 Associate members.

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W. Warner Watkins, M.D., Radiologist

Diplomates of American Board of Radiology

Lorel A. Stapley, M.D., Consultant Pathologist